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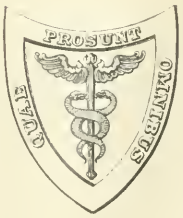

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THE

AMERICAN JOURNAL

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ORIGINAL ARTICLES

POSTOPERATIVE AND POSTANESTHETIC NEURASTHENIAS AND PSYCHOSES.

By John K. Mitchell, M.D.,

PHYSICIAN TO THE PHILADELPHIA ORTHOPEDIC HOSPITAL AND INFIRMARY FOR NERVOUS DISEASES.

There is not and there cannot well be any reliable evidence as to the frequency with which neurasthenias or other forms of mental disturbance follow operations, since the operating surgeon often knows nothing of their occurrence, many of them not making their appearance until weeks or even months after surgical and anatomical recovery is complete. The surgeon's records, therefore, only show such acute troubles as passing deliria, temporary confusion, or aberration, such as sometimes appear directly after operations, and may with probability be referred rather to the anesthetic or to the physical shock than to the operative procedure; some examples of this type are recorded in the accompanying list.

For the purposes of the present discussion, I have made examination of some hundreds of case histories, taken with few exceptions during eight or ten years past. The investigation was limited to this period for several reasons: (1) Because during this time special attention had been given in my case-taking to those instances in which operation was alleged as among the causes of the nervous trouble; (2) because many of the cases within this time are near enough for memory to confirm or criticise the formal notes; and (3) because the histories are much more minute and complete than those of earlier years.

To make clear the basis of the diagnoses, a brief explanation of terms must be made. "Neurasthenia" covers cases of the fatigue-neurosis type, without marked mental symptoms. "Melancholia" is used to indicate instances of nervous depression, often hypochondriac, not including the more serious forms such as might be put under the head of manic-depressive insanity or the recurrent periodic melancholias. "Psychasthenia" has been applied only to cases with obsessions, or *idées fixes*, and those which though superficially seeming neurasthenic exhibited on further study mental disturbances. These are all "revised diagnoses," recorded when patients were discharged, the original titles having been hysteria, hysteroneurasthenia, hypochondriasis, neurasthenia, cerebrasthenia, myelasthenia, or whatever other diagnostic fragments one might choose to chop the general name of neurasthenia into, and intended in practice to serve as temporary signposts pointing to the therapeusis. So far as possible, instances in which distinct neurasthenia was present before operation have been excluded, so that the form in which the record stands fairly represents careful final diagnostic consideration of various mental, psychical, or neurotic disorders consequent upon, if not causally connected with, surgical procedures. Further, only notes of private patients have been used, not even including those treated in private rooms in hospital service, the former being for the most part under closer observation by myself and by experienced assistants, and their histories not depending in any way upon records made by internes, who, however alert and well-trained, have not the same opportunities of personal study of the patients.

Certain definite forms of neurasthenia and psychasthenia have been omitted from consideration altogether, as those of sexual origin, a few in which it seemed possible that beginning paresis or dementia præcox was at the root of the symptoms, several in which the history was too vague and those in which the patient for any reason was not long enough under observation for the certain establishing of the diagnosis.

344 case histories remained after these exclusions, ranged under the several headings named. These were reviewed, with the aim of discovering how many of them could fairly and reasonably be classed as postoperative or postanesthetic troubles.

Total cases examined 344: Women, 220 (or 64 per cent.); men, 124 (or 36 per cent.).

Instances of neurasthenic or mental disorders following operation or anesthesia, 31 (or 9 per cent. of the total cases examined): women, 29 (or 94 per cent. of the postoperative cases); men, 2 (or 6 per cent. of the postoperative cases).

No.	Social condition.	Age.	Year operated.	Operation.	Notes.
1	Female, married	30	1887	Cervix dilatation	Professor Goodell; panic terror preceding operation; violent hysteria following, lasting many years.
2	Female, married	34	1889	Ovariotomy, double	Professor Goodell; mania immediately following operation; death from exhaustion.
3	Female, single	38	1893	Ovariotomy, double	Neurasthenia following; many years' duration.
4	Female, married	36	1899	Ovariotomy	Nervousness preceded; ovariotomy; stump-abscess complication.
5	Female, single	62	1900	Carbuncle and hemorrhoids	Melancholia followed.
6	Female, married	43	1900	Kidney fixation. Curettage, two operations (one year apart)	Hysterical hypochondriasis.
7	Female, single	28	1901	Ovariotomy	Hysteria.
8	Female, married	31	1903	Cervix repair	Neurasthenia, hypochondriae type.
9	Female, married	36	1903	Total hysterectomy	Mother had puerperal insanity; psychasthenia; obsession of guilt.
10	Female, married	55	1898	Hystereetomy Amputation of breast, two operations (five years apart)	Six months after operation, nervous depression began, lasting five years, then breast amputation, followed by increased depression.
11	Female, single	28	1903	Appendectomy	Bad family history of insanity; acute depression.
12	Female, married	32	1896	Perineum repair, 1896; ovariotomy, 1897; hystereetomy, 1902; three operations years apart	Previous health perfeet; neurasthenia.
13	Male, married	..	1904	Appendeetomy	Acute insanity of a few weeks' duration.
14	Female, married	..	1905	Total hystereetomy	Psychasthenia followed.
15	Female, married	36	1899	Two operations; one ovariotomy; then hysterectomy and ovariotomy	Doubtful history of nervousness preceding; hysteria following.
16	Female, married	44	1905	Cervix repairs	No ether given, at patient's desire; hypoehondriae neurasthenia following directly.
17	Female, married	30	1906	Sebaeeous cyst; cervix, kidney fixation	Always nervous, much increased after operation, and finally severe psychasthenia.
18	Female, married	46	1906	Curettage; also two indueed abortions	The abortions added a moral eause, operations perhaps only contributed to the sequent neurasthenia.
19	Female, married	38	1899	Curettage; ovariotomy; suspension; three operations	Neurasthenia; previous health perfeet.
20	Male, married	33	1907	Appendeetomy, 1903; epulid, 1907	Psychasthenia followed first operation, increased by second.
21	Female, married	26	1908	Ovariotomy and nasal septum straigbtened	Neurasthenia; previous health good· gastroptosis.
22	Female, married	57	1908	Hystereetomy for tumor	Neurasthenia.

No.	Social condition.	Age.	Year operated.	Operation.	Notes.
23	Female, single	50	....	Ovariotomy and several ocular tenotomies	Hysteroneurasthenia.
24	Female, married	40?	....	Ocular tenotomy and two curettings	Increasing neurasthenia.
25	Female, married	..	1909	Cervix repair; curettage	Sudden neurasthenia, with depression six weeks later.
26	Female, single	44	1902	Hysteroövariotomy	Previous health perfect; hypochondriac neurasthenia of very obstinate type; endless doctors, psychotherapy, etc.
27	Female, married	28	1909	Appendectomy; hemorrhoids	Neurasthenia; operation during typhoid attack.
28	Female, married	38	1910	Appendectomy	Psychasthenia, hypochondriac ideas.
29	Female, single	40	1910	Thyroidectomy and two operations on hemorrhoids	Always nervous, but never neurasthenic before operation.
30	Female, married	20	1910	Appendectomy; acute, first attack	Neurasthenia.
31	Female, married	26	....	Ether, no operation	Delusion of criminal assault.

The dates refer to the year in which operation was done, but with few exceptions the histories of the cases were taken during the years from 1898 to 1910.

Of these 31 cases, 29 are from the full case histories, selected by the process of elimination described as fairly representing instances of postoperative trouble. With these 29 are included one case of my own, of which I find no complete statement in my archives, but of which memory supplies a very distinct record, and one supplied by Dr. Weir Mitchell, Cases 2 and 31 respectively.

The operations in these cases varied very widely, from the most trifling surgical intervention, such as ocular tenotomy, straightening of the nasal septum or dilatation of the cervix uteri, up to total hysterectomy and ovariotomy.

The sex distribution is rather striking. Although aware that the proportion of male patients with serious neurotic symptoms was a large one, it was rather unexpected to find it more than one-third of the total. It is interesting to observe that this close equality in the incidence of neuroses is not maintained in the cases suffering from postoperative disorder, in which males have a very small share. The comment of course suggests itself that diseases of the female reproductive organs account for a large number of the operative cases. The males represent but 2 in the total of the 31 instances of postoperative mental disturbances, and these 2 amount to less than 0.5 per cent. of all the cases examined. While not directly connected with the subject, it is worth adding that in the total case histories examined in making up this list the proportion of male cases gave 41 per cent. of the neurasthenias, 25 per cent. of

the melancholias, and 41 per cent. of the psychasthenias, although all instances of sexual neurasthenias and obsessions were strictly excluded.

The worse and most persistent examples of nervous disorder have not by any means always followed the most serious operations. No doubt, as in other neurasthenic conditions, a certain constitutional or temperamental predisposition is required as a precedent, and one cannot make a rule excluding this as one of the causes, as one would in judging of purely traumatic neuroses; but I have tried to exclude from the list those in which there were marked and distinct causes other than operative in addition to the neurasthenic predisposition. Bodily shock or severe pain are not evidently among the necessary causes of this condition. The mental or nervous factors, particularly fright, play a larger part than is generally attributed to them, I feel sure. We practitioners are so accustomed to operations that we do not always allow for the alarm of patients, and treat their fears too lightly.

Complications in the surgical course of the cases seem to have played no part, as in only one instance (No. 4) was any such trouble reported, and in many it was particularly stated that progress had been uninterrupted. Nor can reckless or careless surgery be charged with the unfortunate results, for if it were possible to publish the operators, many distinguished names would be found in the list, whose positions would sufficiently guarantee that care had been used and every precaution taken, both in the selection and treatment of the cases.

Two or three of the cases collected are sufficiently interesting for brief separate comments, as they teach highly instructive lessons.

In one, No. 31, a young woman, a widow, went to a dentist's office with her mother and her attending physician, with the intention of having two teeth extracted under ether. When the administration was begun she struggled and fought so wildly that her mother would not consent that the attempt at anesthization should be continued. The administration ceased before complete relaxation was produced, and no operation of any kind was performed. When the young woman came out of her ether intoxication she asserted with every evidence of the fullest belief that she had been assaulted during her stupor, and this delusion, in spite of every assurance of her mother and of the physician, who had never left her side, persisted very strongly for several weeks, and then gradually faded.

No. 1, seen many years ago with the late Professor Goodell, was etherized for dilatation of the cervix. She was an intelligent woman of education, and had the matter fully explained to her, but was in great fear of the anesthetic. The operation was done briefly, with no violence. When she recovered from the anesthetic

she was in a condition of extraordinarily severe hysteria, and continued for twenty years to exhibit one after another an amazing series of hysterical phenomena; and, indeed, up to the time of her death never recovered complete mental balance and control.

In another case, No. 2, operated upon by Professor Goodell, a difficult ovariotomy with adhesions, requiring rather long etherization, the patient, who had been in a perfectly good mental state before the operation, was wildly maniacal after the ether, and continued in a state of furious mania until her death from exhaustion, about two weeks later.

No special investigation was made in the earlier instances as to the actual time spent in bed after operation, but in the later ones this question has been systematically inquired into, and has usually been answered by the statement that the patient was up at the earliest possible time. I am not unaware that there are good surgical reasons for getting patients out of bed, particularly after abdominal operations, as soon as may be; but I am strongly of opinion that troubles of the kind we are discussing would be less frequent if, instead of trying to get the patient up as soon as possible, the period of rest in bed and mental repose—of course, with general treatment, massage, and perhaps bed gymnastics—were rather to be extended than curtailed, an opinion borne out by personal experience gained in watching the numerous instances in which it has been necessary to have operations performed upon patients either already neurasthenic or at least with the temperamental tendency toward nervous disorders. Under these circumstances, it has been my custom to insist upon a more prolonged rest and isolation than would be considered necessary for purely surgical reasons, and with excellent results in avoiding postoperative nervous complications.

The statements of patients as to physicians' opinions we all know must be received with the utmost skepticism, so that we may to some extent discount the assertions quite frequently made that relief from neurasthenic symptoms had been held out as a reason for operating; but in many instances there has been additional testimony confirmatory of the patient's reports, in some coming from surgeons themselves on this point.

This leads to a warning which may be addressed both to the physician who, desperate over the lack of success of his treatment of a neurasthenic woman, turns for aid to his surgical colleague and also to that invaluable coadjutor. Should the question of surgical treatment of a neurasthenic person arise, much more than the ordinary care must be exercised in deciding upon operation. Wise practice will choose any other route than a surgical one, however roundabout it may make the journey. The only sufficient reason for an operation in a neurasthenic is that the procedure is one which would be absolutely demanded were the patient in

perfect nervous health. The physician and the consulting surgeon must never be deceived into undertaking an operation for the relief of neurasthenic symptoms, unless these symptoms would require, imperatively require, surgical measures in a person not nervous. An operation may relieve neurasthenic symptoms; it will not cure the patient, and there is a good chance that a few months will see her worse than ever, having gained nothing but a new experience, and very likely an exchange of old symptoms for new ones. We should think twice before advising an operation on a neurasthenic, and having thought twice it will often prove best to think a third time, and then not operate. Above all, the operation should never be recommended with the idea or even the hope that if successful it will cure the neurasthenic. The neurasthenia may be no worse after than before; but most assuredly it will very, very seldom be cured.

A STUDY OF THE NITROGEN METABOLISM IN THREE CASES OF DUODENAL ALIMENTATION.

By Max Einhorn, M.D.,
and
Jacob Rosenbloom, M.D., Ph.D.,
new york.

(From the Wards and Chemical Laboratory of the German Hospital, New York City, and the Laboratory of Biological Chemistry of Columbia University, at the College of Physicians and Surgeons, New York City.)

As is well known, it is impossible to maintain the nitrogenous equilibrium in patients kept under rectal alimentation. This deficiency greatly impairs the utility of that method of feeding. One of us has accordingly devised a new mode of feeding subjects in whom absolute rest for the stomach is demanded, viz., by introducing the food directly into the duodenum with a duodenal pump.

By the new method a duodenal pump is inserted directly into the digestive tract and left there for two weeks. As soon as the end of the pump has reached the duodenum, nourishment can be injected into the latter.[1] The food can thus be conveyed into the duodenum at desire and the stomach can be kept entirely free from contact with the food.

While clinically this method of feeding was found to be wholly

[1] A full description of the method of introducing the food, and of the clinical history of the patients whose nitrogen metabolism was determined under this method of feeding, may be found in the following papers: Einhorn, Zeit. f. Physik. und diät. Therapie, 1910, xiv, 452; Interstate Med. Jour., 1910, xvii, 758.

TABLE I.—Miss S. Typical case of gastric ulcer. The weight of the patient at start of treatment was 116½ pounds. The duodenal pump was inserted on April 14, 1910, and feeding was started on April 15. The pump was removed on April 28. The weight at the end of the treatment was 114 pounds.

Date, 1910.	Total nitrogen.			Urine.								Feces.	
						Urea N.		Ammonia N.		Uric acid N.			
	Ingested.	Excreted.	Balance.	Volume.	Total N.		Percentage of total N in urine.		Percentage of total N in urine.		Percentage of total N in urine.	N	Percentage of total N ingested.
	grams.	grams.	grams.	c.c.	grams.	grams.		grams.		grams.		grams.	
April 20	16.2	11.47	+4.73	1370	9.97	8.3	83.25	0.445	4.47	0.35	3.51	1.5	9.26
April 21	15.9	13.11	+2.79	2115	11.61	9.71	83.64	0.474	4.09	0.42	3.61	1.5	9.43
April 22	15.8	13.47	+2.33	1620	11.97	10.04	83.88	0.290	2.42	0.37	3.09	1.5	9.49
April 23	15.2	14.92	+0.28	1480	13.42	11.98	81.82	0.962	7.18	0.48	3.58	1.5	9.87
April 24	16.0	16.48	—0.48	1120	14.68	12.54	85.42	0.502	3.42	0.36	2.45	1.8	11.25
April 25	15.2	13.34	+1.86	1030	11.54	9.96	86.31	0.368	3.13	0.30	2.60	1.8	11.84
April 27	16.3	16.34	—0.04	1250	14.54	12.60	86.66	0.52	3.57	0.37	2.54	1.8	11.04
April 28	16.4	19.21	—2.81	1340	17.41	14.52	83.45	0.62	3.56	0.41	2.35	1.8	10.98
Totals	127.0	118.34	+8.66										
Average	15.875	14.792	+1.08										

TABLE II.—Mr. B. Typical case of gastric ulcer. The weight of the patient was 132 pounds on June 25, 1910. The tube was inserted on June 23, and feeding was started on June 24. The tube was removed on July 7. At the end of the treatment the patient weighed 132 pounds.

Date, 1910.	Total nitrogen.			Urine.						Feces.	
						Urea N.		Ammonia.			
	Ingested.	Excreted.	Balance.	Volume.	Total N.		Per cent. of total N. in urine.		Per cent. of total N. in urine.	N.	Per cent. of total N. ingested.
	grams.	grams.	grams.	c.c.	grams.	grams.		grams.		gms.	
June 28	17.2	16.58	+0.62	1450	15.08	12.55	83.2	0.78	5.2	1.5	8.72
June 29	16.2	16.46	—0.26	980	14.96	12.64	84.5	0.73	4.9	1.5	9.25
June 30	15.9	15.22	+0.68	1420	13.72	11.89	86.7	0.70	5.1	1.5	9.43
July 1	17.4	16.36	+1.04	1640	14.86	12.75	85.8	0.70	4.7	1.5	8.62
July 2	16.4	16.33	+0.07	1280	14.83	12.79	86.1	0.78	5.3	1.5	9.14
July 3	16.4	15.27	+1.13	890	14.07	11.85	84.2	0.65	4.6	1.2	7.31
July 4	16.2	16.40	—0.2	1380	15.20	12.74	83.8	0.62	4.1	1.2	7.41
July 5	14.5	16.12	—1.6	1900	14.92	12.64	84.7	0.60	4.7	1.2	8.27
July 6	16.4	15.66	+0.74	1810	14.46	12.30	85.1	0.71	4.8	1.2	7.31
July 7	16.1	16.08	+0.02	1280	14.88	12.63	84.9	0.76	5.1	1.2	7.45
Totals	162.7	160.48	+2.22								
Average	16.27	16.048	+0.222								

TABLE III.—Mr. F. Typical case of gastric ulcer. The weight of the patient at the beginning of the treatment was 146 pounds; at end, 146 pounds. The tube was inserted on June 14, and withdrawn on June 28.

Date, 1910.	Total nitrogen.			Urine.						Feces.	
						Urea N.		Ammonia.			
	Ingested.	Excreted.	Balance.	Volume.	Total N.		Per cent. of total N. in urine.		Per cent. of total N. in urine.	N.	Per cent. of total N. ingesetd.
	grams.	grams.	grams.	c.c.	grams.	grams.		grams.		gms.	
June 17	15.5	16.33	—0.83	595	14.93	12.80	85.8	0.48	3.2	1.4	9.03
June 19	15.5	15.16	+0.34	565	13.76	11.30	82.1	0.51	3.7	1.4	9.03
June 20	16.4	16.80	—0.4	630	15.40	13.16	85.4	0.48	3.1	1.4	8.54
June 21	16.3	13.51	+2.79	445	12.11	10.40	85.9	0.47	3.9	1.4	8.59
June 24	16.4	15.31	+1.09	650	13.91	11.60	83.4	0.62	4.4	1.4	8.54
June 25	16.6	14.16	+2.44	730	12.86	11.08	86.2	0.38	3.0	1.3	7.83
June 26	16.4	14.70	+1.7	870	13.40	11.40	85.1	0.58	4.3	1.3	7.93
June 27	16.2	14.22	+1.98	860	12.92	10.98	84.9	0.54	4.2	1.3	8.02
June 28	16.0	12.72	+3.28	940	11.42	9.71	85.0	0.56	4.9	1.3	8.12
Totals	115.3	132.91	+12.39								
Average	16.144	14.767	+1.376								

satisfactory, it remained to be seen whether a perfect nitrogenous equilibrium could be maintained, and whether the protein food was assimilated in a normal manner. In order to decide these points we have made analytical studies of the nitrogen intake and output in three patients who have been kept on duodenal feeding, each for a period of two weeks.

All of the patients suffered from ulcer of the stomach. In one the ulcer was situated near the cardia. In the two others the ulcer was situated in the lesser curvature of the stomach, and was complicated with pylorospasm, leading to temporary ischochymia. As a rule, we gave eight ounces of milk, one raw egg, and one or two tablespoonfuls of lactose, the mixture being well mixed and strained before introduction. At each feeding the patient received the above amount of food, at intervals of two hours, eight times daily. When there is intolerance to this quantity of nourishment for each feeding half the quantity may be given every hour. This was the case in one of our patients throughout the treatment, and in another at times. In one of them (Mr. F.) the lactose had to be omitted on account of the great irritability of the enteric tract on account of an existing colitis.

Tables I, II and III contain the results obtained by the examination of the urine and feces of these patients. Samples of the milk given to these patients were analyzed for its daily nitrogen content. The nitrogen of the weighed eggs (minus shell) was computed with the aid of the figures given by Koenig (2.008 per cent. N). The feces were marked off by means of carmine into periods of four to five days.

Nitrogen determinations were made by the Kjeldahl method, the ammonia by the Folin method, urea by Benedict's new method (*Jour. Biolog. Chem.*, 1910, viii, 405) and uric acid by the Folin-Schaffer method.

Table IV.—Summary of data pertaining to total nitrogen metabolism (Tables I to III).

	Ingested grams.	Excreted grams.	Balance grams.
Table I	127.0	118.34	+8.66
Table II	162.7	160.48	+2.22
Table III	145.3	132.91	+12.39
Average	145.0	137.24	+7.76
Average daily	16.11	15.25	+0.86

It can readily be seen that in these three cases of duodenal alimentation the absorption of the nitrogen of the food took place to a normal extent. Nitrogenous katabolism, as measured by the quantities of urea and ammonia that were excreted, was normal in degree. All of the patients had a positive nitrogen balance throughout the duodenal feeding periods.

THE DILATATION TEST FOR CHRONIC APPENDICITIS.

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That many persistent digestive disturbances are manifestations of a latent or chronic appendicitis has been repeatedly demonstrated by the disappearance of the disturbances after the removal of the appendix. It is also well-known to operators that in some of these cases the appendicitis was not recognized for a long time, and that even after long observation there were cases in which there was a large element of uncertainty as to whether the appendix was involved or not. In other words, the appendicitis was latent, and could not be detected by the ordinary means of examination. Hence any measure by which such a latent appendix involvement can be recognized deserves consideration. We would, therefore, again call attention to the usefulness of dilating the colon with air to determine the presence or absence of a latent or chronic appendicitis. Since our first report of the test, we have applied it in a large number of abdominal cases, and have been able in a number of instances to establish the diagnosis of appendicitis when all other methods of examination failed completely or left the examiner in a state of reasonable doubt. In addition, we have received verbal reports from several surgeons who have been employing the test as a routine in their hospital cases. In their experience, as well as our own, the test as checked by operation has proved reliable, failure being reported in only four or five cases in several hundred.

To make the test a colon tube is passed eleven or twelve inches into the rectum and air injected by means of an atomizer bulb. If, as the colon distends, pain and tenderness to finger-point pressure become apparent at McBurney's point, there is appendicitis. We have compared the test in a number of instances with the Rovsing test and find this much the more certain; but at times, after moderate dilatation with air, the Rovsing method of forcing the air back into the cecum may be used with advantage. We might sound a warning that if most of the air is not allowed to escape before withdrawal of the tube, colicky pains are likely to ensue.

The test is not needed in an acute case, and in such would be contraindicated; neither is it required in an undoubted chronic case. But the indication for the test is a suspected chronic or latent appendicitis, or any persistent digestive or abdominal disturbance, in which no cause can be found for the trouble. Ordinarily one may entertain doubt about the diagnosis, or at least hesitate about urging operation, when tenderness at McBurney's point can be

elicited only on very deep pressure, or is accompanied by a similar tenderness elsewhere in the abdomen. At times, for example, we have thought of appendicitis because of McBurney's point tenderness, but have found in addition puzzling points of tenderness along the transverse colon or at a spot on the left side corresponding with McBurney's. In such cases, dilatation frequently results in the disappearance of all the points of tenderness except that at McBurney's, which it intensifies.

Again, in persistent cases of hyperchlorhydria or gastrosuccorrhea the test should be performed. For just as in the case of a gall-bladder, so a latent appendicitis may have its chief manifestation in stomach derangement, even so marked at times as to simulate an ulcer. And since it has become our routine practice to dilate the colon in all long-standing cases of the kind, we have had the good fortune in a number of instances to discover an unsuspected appendix and to see the gastric symptoms disappear with the removal of the offending vestige.

A further application of the test may be to distinguish between an inflamed appendix and a right-sided pelvic trouble. Pain and tenderness in a right-sided chronic salpingitis or cystic ovary sometimes result from the colon dilatation, but the tenderness is regularly less acute, is low down in the abdomen, and extends toward the middle line. In three instances we have been able to diagnosticate pelvic inflammation in young women in whom appendicitis was suspected and in whom a vaginal examination was impossible except under ether. In each of these the subsequent operation revealed a cystic right ovary and a free uninvolved appendix. We have employed the test in not a few other gynecological cases, and while in some we have been able merely to corroborate the findings of a vaginal examination, in others we have demonstrated appendicitis in addition to the pelvic lesion. In every such case operated upon the finding of the dilatation test has been found correct.

A few typical case reports may be of interest:

Case I.—G. L., painter, has had attacks of pain in the abdomen at intervals for one and one-half years, without nausea or vomiting. Recently such attacks have become more numerous, and in the last, he had to lie down for one afternoon; he was told he had painter's colic. He told us that the pain occurred mostly just above the umbilicus or high up beneath the right ribs. He had no lead line on the gums, no polychromatophilia in the blood. On colon dilatation, the gall-bladder was not made out, and no pain appeared in the hepatic region; but in two spots there were pain and tenderness, one spot just at McBurney's point and another just below the navel. A small umbilical hernia also made its appearance. The patient was advised to have an operation for the hernia and the appendicitis, but as the diagnosis was not confirmed by others he

was treated for three months for lead poisoning, intestinal indigestion, and rheumatism. The attacks, however, increased and were more localized in the appendix region, so he returned for operation. The dilatation test was again positive, and operation was performed by Dr. H. H. M. Lyle. The chronically inflamed appendix was covered by veil-like adhesions, which extended to the hernial opening; the gall-bladder contained no stones. The appendix and the adhesions were removed and the hernia closed. The patient has had no more attacks of the old type, and a little recurrence of the pain beneath the right ribs disappeared quickly under treatment for hyperchlorhydria.

Case II.—D., a physician, in two years had five attacks of severe pain in the abdomen, with prostration and vomiting. The pain was always diffuse, never localized, and lasted about one day; the temperature never rose above 99° F., and the pulse was normal or slow. Physicians had suggested appendicitis, but no positive diagnosis was made. Two days after the last attack, which was so severe that morphine had been administered, the patient walked to my office apparently well. Slight tenderness to finger-point pressure at McBurney's point could be elicited only on very deep pressure, but on dilating the colon an acute pain appeared in the appendix region, and tenderness over an area as large as a silver dollar and centring over McBurney's point. Four days later, Dr. J. A. Blake operated and found a chronically inflamed appendix with a constriction close to the cecum, and adhesions extending upward over the cecum. The patient has had no attack since the operation (not quite a year).

Case III.—Mrs. R., twelve years ago, had an attack of pain in the abdomen, with vomiting, and was in bed one day. A surgeon saw her in the attack, and said it was not appendicitis. During the entire twelve years since then she has taken a laxative pill every night and has had no further severe pain, but for the last six months has been losing appetite and becoming more costive, and has been irritable and in low spirits. A month ago had a little abdominal pain on the right side for one day, but not enough to require treatment. A test breakfast showed free hydrochloric, 48; total acidity, 70. No organic acid. On dilatation of the colon, pain at McBurney's point with sharply localized tenderness became manifest. It was our belief that hyperchlorhydria treatment would be futile in the presence of a chronic appendicitis, so operation was advised, and Dr. L. W. Hotchkiss removed a retrocecal swollen appendix with three marked constrictions and surrounded by adhesions. Since the operation, eight months ago, the patient has had unusually good digestive and bowel functions and has been in excellent general health and spirits.

Case IV.—Miss H., aged twenty-four years, a rather underdeveloped young woman, with a mitral stenosis, has had in the

last year several attacks of cramp-like pain in the right iliac region. Two or three times this pain came at the menstrual period, but occurred also at other times. Vaginal examination was not feasible, so the colon was dilated. At once there was a dull pain over the whole lower right segment of the abdomen, extending from McBurney's point to Poupart's ligament and to the midline. Tenderness was slight, and was most pronounced about half way between McBurney's point and the symphysis pubis. Operation by Dr. H. T. Goodwin showed a right ovarian cyst and a normal appendix.

Case V.—Miss G., aged twenty-seven years, has had pain in the right side low down for a year or more. It has never been very acute, never caused vomiting, and was most pronounced after the patient had been a long time on her feet. There has been a rather abundant vaginal discharge. Examination per vaginam reveals a tender boggy mass in the right fornix, and much tenderness when the uterus is moved. Out of curiosity, the colon was dilated, and to our surprise an acute pain appeared in the appendix region, and tenderness localized at McBurney's point. Operation by Dr. Frank Markoe showed right salpingitis with tube, ovary, and chronically inflamed appendix bound together in a mass of adhesions.

Case VI.—D. S., has never had any acute attack of appendicitis, but has had some pain in the appendix region when his bowels seemed full of gas. Dilatation was positive for appendicitis. Some time later, in Chicago, he had an acute attack which was diagnosticated appendicitis, and though prostrated and with fever, he took train immediately for New York. Dr. H. H. M. Lyle operated and found a retrocecal abscess with a sloughed off appendix.

These cases illustrate the positive findings of the dilatation test. In the use of the test during the last four years we have had no case in which the test was positive and the operation findings negative. But in two out of all of our cases, the negative finding of the test was followed within six months by a typical attack of appendicitis, and the test was, therefore, presumably at fault. Several times in the early days of the test surgeons operated for a suspected appendicitis, though the test was negative, and in every such case the appendix was found normal. We have had a verbal report from one surgeon, who has used the test extensively, of two cases which gave positive test but negative findings at operation. With very few exceptions, therefore, the test has proved accurate, and it may well serve as a guide to the necessity for operation, particularly in the three classes of cases mentioned, viz., suspected chronic appendicitis, persistent gastro-intestinal or abdominal disturbance with unknown cause, and appendicitis versus ovarian or tubal inflammation.

ACQUIRED DIVERTICULA OF THE SIGMOID, WITH A REPORT OF SIX CASES.[1]

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AND

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At the Twenty-seventh Congress of Surgery, Graser demonstrated a stenosis of the sigmoid due to chronic hyperplastic inflammation, on which an operation for cancer had been performed. He believed the portal of entrance for the infection to be a number of acquired diverticula, some of which were seen entering the inflammatory mass. From Graser's paper dates the clinical interest in the subject, for before that time diverticula had been considered merely pathological curiosities. They had been described by Morgagni (1796), Fleischmann (1815), Albers (1844), Habershon (1857), Klebs (1869), Loomis (1872), Fischer (1900), and others.

Acquired diverticula are of two varieties, the true and the false. True diverticula are merely wide-mouthed pouches whose walls contain all of the layers of the normal bowel. They are the result of an abnormal tendency to haustrum formation, and seem to be of anatomical significance only. False diverticula, on the contrary, are herniaform protrusions of the mucous membrane through the muscularis, and are of increasing clinical and pathological moment.

Acquired diverticula may occur throughout the entire intestinal tract. They have frequently been seen in the duodenum in the vicinity of Vater's papilla. They are common in the colon, and they cease abruptly at the first portion of the rectum. Occasionally they have been observed in the appendix, where they may be the seat of a condition which cannot be differentiated from appendicitis. They vary in number from several hundred (400, Hansemann) to an isolated protrusion. They are generally multiple.

Since diverticula of the sigmoid are much more likely to give rise to clinical manifestations, your attention will be directed toward them only.

Etiology. Their origin is still a mooted question. A predisposition to diverticulum formation undoubtedly exists, and according to Graser and Sudsuki is common. On microscopic examination of the sigmoid in old subjects, the former found small diverticula in 10 out of 28 cases, and the latter in 15 out of 40 cases.

[1] Read before the Cincinnati Society for Medical Research, February 24, 1910.

The following theories as to cause have been suggested:

1. That the fenestra through which the vessels penetrate the muscularis form *loci minoris resistentiæ*. The vessels are surrounded by loose connective tissue which contains a variable amount of fat. As the individual ages, the fat increases, the connective tissue becomes weaker, and the fenestra are increased in size by atrophy of the muscularis. Intermittent stasis also stretches and increases the diameter of the fenestra. During periods of cessation of stasis, the caliber of the vessels diminish, and loose space in the "vessel holes" results. These factors increase the predisposition. Accumulation of feces and gas incident to constipation, bowel atony, and abnormal decomposition act to a degree as determinining factors. The vascular theory is accepted by Fischer, Koch, Hansemann, Berner, and others, and is corroborated by four of the cases which we studied microscopically.

2. Bland-Sutton believes that the appendices epiploicæ form points of lessened resistance because, as he has shown, their fat is in immediate continuity with the subserous fat of the intestinal wall. It is difficult to see, however, why continuity of fat should predispose to diverticula. The process is that of a penetration of the muscularis, and it seems highly improbable that the weak serosa, and its subserous layer of fat, could play any part in it. It is more probable that the fact that bloodvessels penetrate the muscularis at this point is the chief reason for the common incidence of diverticula here. In some cases an adherent appendix may cause the production of traction diverticula.

3. Franke believes that developmental anomalies are at the basis of diverticulum formation. What these developmental imperfections are he leaves unspecified.

4. Beer and Telling consider weakening of the muscular coat in adult life as the chief cause of diverticula. They do not state why the muscular wall should weaken in certain spots and not in others. They assume that the vessels may "direct the path" for the diverticula. Beer states: "The fact that diverticula occur in old people, in people whose intestines have been more or less worked out, as evidenced by constipation, points to a muscular deficiency, and in this muscular weakness the cause of false diverticula must be sought."

5. Age seems to be to some extent a determining factor. In 80 cases the average age was sixty years (Telling). Forty-seven of the 80 cases gave rise to clinical symptoms at the average of fifty-five years. The ages of our 6 cases were as follows: Without symptoms, 75, 78, and unknown; with symptoms, 83 (symptoms due to cicatricial stenosis secondary to diverticulitis), 45, and 50.

6. Sex also plays a part. Of 81 cases, 53 were male, 28 female (Telling). Our 6 cases were all men.

7. Obesity has been emphasized as a causative factor by Klebs, Mayo, and others, but it seems to be only an indication of involution

processes and thus only a concomitant of weakness in the muscularis or in the "vessel holes." Only 2 of our cases showed any unusual increase in fat.

8. Cachexia and absence of fat were marked in one of our cases. It might be inferred that in individuals who had been obese the loss of fat would tend to weaken the intestinal wall by leaving unoccupied or loose spaces.

9. The physiological role of the sigmoid must be of some moment in promoting diverticulum formation. The feces are retained longest in this segment (average ten to twenty-four hours), and its walls are incessantly subjected to changes in pressure due to variations in the quantity and quality of its contents, and so a predisposition and tendency to atony is inherent in the normal function of the sigmoid.

10. When the physiological retention of feces becomes excessive and constipation arises, the strain upon the gut walls is abnormal and any tendency to atony is aggravated. Localized weakenings are subjected to a determinative factor. The causal relationship of constipation to diverticulum formation so often observed might seem to support this view. Fischer's doubts as to the importance of constipation, however, are well founded. Its role has certainly been exaggerated and cases are numerous in which constipation has not been recorded. Only a very small proportion of the constipated have diverticula. Abnormal decomposition of retained contents with gas production is probably of more moment. Constipation, if it plays a part, must apparently be of the atonic type. The writers know of no investigation as to this point. Any factor, however, that will increase intrasigmoidal pressure must influence the development of diverticula at points of lessened resistance.

We may briefly summarize the etiological factors, all of which may be present to a variable extent in every case, as follows: (1) Congenital or acquired anatomical predisposition to localized weakness in the wall of the gut. (2) The addition of certain positive mechanical factors to the above potential factors, viz., (*a*) Strain on the bowel wall due to the accumulation of gas and feces. (*b*) Changes in the caliber and structural strength of the "vessel holes" consequent on stasis and senile circulatory disturbances, or on rapid loss of visceral fat. (*c*) Atony, which may be due to age, distention, or obesity.

Pathology. There is little definite information on the postmortem incidence of acquired diverticula of the sigmoid, for, as a rule, little attention is given to this segment of the gut in the routine autopsy, unless clinical manifestations or conspicuous pathological alteration draws the attention thither. In 78 cases in which the sigmoid was carefully examined by us at the autopsy, acquired diverticula were found five times. Two of the above cases were clinical. In one, the diagnosis was suspected almost to a certainty,

in the second, it was a "find." The remaining cases were discovered because they were looked for.[2] False diverticula are usually situated near the mesenteric attachment. According to Bland-Sutton, Franke, and Telling, they are most commonly formed at the appendices epiploicæ. In three of our autopsies they were located at these points. In one case their location was at the mesenteric attachment. In one case, the diverticula were located in the vicinity of the appendices, but their relationship to them could not be determined on account of the hyperplasia of the gut wall and an inflammatory infiltration of the immense amount of fat surrounding the sigmoid. One peculiarity in this case not hitherto noted is the location of the diverticula on the summits of the rugæ, where they were discovered as minute depressions only after careful search. One of these innocent-looking depressions led into a fistulous tract. Location opposite the mesenteric attachment has been described by Hansemann.

The *size* of *acquired diverticula* varies from minute herniaform protrusions of the mucosa, discoverable only with the microscope, to processes the size of peas or grapes. (Size of an apple—Edel; of an egg—Virchow). They are conical, sacular, spherical, or teat-like processes

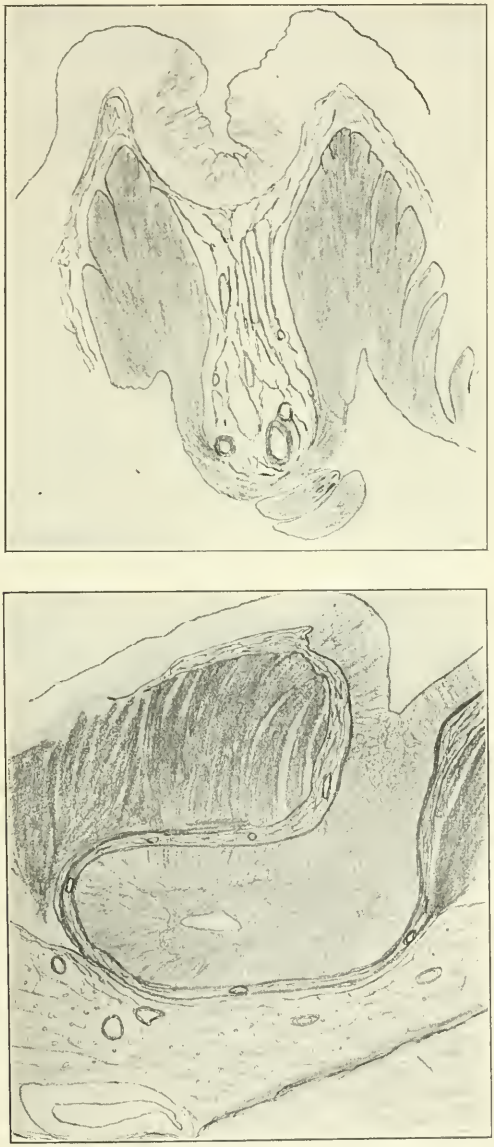
The ostia vary markedly in size. Sometimes the diameter of the opening equals that of the average diameter of the diverticulum. Often the openings are narrow, and although one easily discovers the pouch on the outer surface of the bowel, the mucosa must be scanned carefully to find the mouth. Many of them are distinctly flask-shaped, and their necks seem to be constricted by the penetrated musculature. This shape is especially characteristic of diverticula into the appendices epiploicæ, and creates an excellent mechanism to prevent drainage. Catarrhal inflammation may easily cause edema and swelling of the mucosa, and thus completely occlude the neck. Thus, there is formed a thin-walled sack filled with infectious material lying outside of the gut. The peritoneal cavity is protected only by a thin membrane consisting of mucosa, serosa, and possibly a few attenuated muscle fibers. The mucosa itself is often eroded or atrophic. It may be completely denuded. Localized foci of infection are common.

The coats of the diverticulum vary. Mucosa, submucosa, and serosa are constant. The amount of muscularis varies in different diverticula, and in different parts of the same diverticulum. The walls are thinnest at the tips of the processes.

Here there may be nothing but a thinned outer layer of mucosa and serosa. In our sections the penetration of the muscularis is clear, even though the diverticulum carries some muscle fiber with

[2] Since the above was written one case has been found in the pathological service of Dr. Woolley in the Cincinnati Hospital, the first observation in 103 autopsies. No symptoms were referable to the diverticulum.

it. The contrast in the thickness of the muscular coating of the diverticulum, and of the layers through which it passes, is most



FIGS. 1 and 2.—Sketches (camera-lucida) to show the development of false diverticula.

marked (Figs. 1, 2, and 3). This accumulated musculature at the neck is suggestive of a sphincter. Beer and others have suggested

that the origin of this picture is a localized weakening of the muscularis, but this still leaves an explanation to be explained. The potentiality for mischief which lies in these structures is evident from an inspection of the sections shown with the description of our cases.

The morbidity from false diverticula depends on the following factors:

1. Thinning of the coats.
2. Ulcerative and perforative action of retained concretions and feces.
3. Presence of pathogenic microörganisms.
4. Defective drainage due to: (*a*) Lack of an effective muscular coat. (*b*) Closure of the neck by edema of the mucosa secondary to colitis or stasis. A mild catarrhal colitis may occlude the openings, and thus result in the formation of a pocket of infectious

Fig. 3.—Sketch (camera-lucida) to show the development of a false diverticulum.

material, from which the peritoneal cavity is poorly protected by a coat of variable thinness. (*c*) Strangulation of the opening by kinking, torsion, or muscular (sphincter) action.

The following morbid processes, due to acquired diverticula of the sigmoid have been noted:

1. *Local Peritonitis.* Cases have been reported in considerable number. Abscesses in the left iliac fossa have frequently been drained and attributed to various causes, such as left-sided appendicitis, infected appendices epiploicæ, colonic ulceration, etc. This is probably the most frequently observed clinical manifestation of diverticulitis. (Telling collected 24 cases.) One of our cases was of this type.

2. *Acute General (Diffuse) Peritonitis.* (*a*) With perforation, 14 cases (Telling). (*b*) Without perforation. Loomis (1872) reports

a single case of general peritonitis in which diverticula were present in large numbers. He assumed that the infection traversed the thin wall of a diverticulum without rupture.

3. *Chronic Hyperplastic Sigmoiditis.* Within the last few years a number of cases have been reported, characterized by a productive inflammation of the sigmoid, which manifests itself by disturbed function of the lower bowel; pain, intermittent and colicky in character; tenderness; and constipation, often spastic in type and frequently alternating with diarrhea. Mucus and occasionally a trace of blood are present in the stools. Examination showed tenderness in the left iliac fossa with a movable sausage-shaped tumor. Recent observations prove a large percentage of these cases to be the result of diverticulitis and peridiverticulitis. Patel says: "Peute-être un jour sera-t-on droit de dire que dans presque tous ces cas decrites sous le nom de sigmoiditis, il s'agit de véritables divérticulites, absolument comme l'appendicite a été substituée peu à peu à la typhlite." There is little question but that many of the successful resections of the sigmoid for carcinoma have been cases of infiltrating sigmoiditis. A review of museum specimens (Mayo, Wilson, Telling, etc.), is already putting certain excised cancers of the sigmoid into this class. Such reports will increase in frequency as the condition becomes better known.

4. *Cancer.* Four cases are reported by Hochenegg, Stierlin, Telling, and Wilson,[3] in which cancer has developed on the basis of a sigmoiditis and perisigmoiditis secondary to chronic diverticulitis. The low grade of prolonged inflammatory irritation which so often precedes carcinoma elsewhere is here produced by a chronic diverticulitis.

5. *Stenoses.* These are the result of inflammation in the intestinal wall. Usually they are caused by a productive inflammation, *i. e.*, sigmoiditis and perisigmoiditis which narrows the lumen of the gut. The mucosa is thrown into folds, but, as a rule, is not ulcerated. Cicatricial contraction following a diverticulitis may produce stenosis, as is clearly shown by one of our specimens. Telling reports the only other case in the literature.

6. *Adhesions.* Adhesions produce symptoms by: (*a*) Traction and constriction. The obstruction is commonly due to the fact that the small bowel becomes adherent to the inflammatory area. (*b*) Adhesions of the gut to the bladder with vesicosigmoidal fistula. Telling found adhesions reported sixteen times and fistula eleven times.

7. *Chronic Mesenteritis.* Riedel, Brehms, Ries, Simpson, and Gardinier have called attention to the probable importance of sigmoid diverticulitis in the production of retraction and shortening

[3] Donald MacCrae, of Council Bluffs, in a personal communication, reports another case in which he excised a carcinoma of the sigmoid which was penetrated by numerous diverticula and which showed the carcinoma developing in inflammatory tissue.

of the sigmoid mesentery, a state which predisposes to volvulus. One of our cases was of this type.

8. *Metastatic Suppuration.* Whyte (1906) has reported the only case of this type. A limited necropsy disclosed multiple abscesses of the liver. The original focus was supposed to be an inflamed diverticulum of the sigmoid containing a fecal concretion.

9. *Perforation Into a Hernial Sac.* Stierlin has reported a case of suppuration into a hernial sac from a perforated diverticulum in an incarcerated sigmoid.

Case I.—B. G., male, aged forty-five years. The family history is negative, and the personal history also until one and one-half years before the present illness, when the patient had an attack of pain and distress in the hypogastrium, with temperature. There was some diarrhea and tenesmus. Constipation was not present at any time. He went to bed for several days on a restricted diet and recovered rapidly.

Except a few fleeting pains and an occasional sense of fulness in the lower quadrants, which disappeared with catharsis, nothing of moment occurred for one and one-half years, when, after a few days of indefinite distress in the hypograstrium, he suffered severe pains in the lower abdomen, which were accompanied by dizziness, faintness, chill, temperature of 103°, and later sweating. The bowels had been free, but with some griping and soreness. The patient went to bed on a restricted diet, and for several days had an irregular temperature, ranging from 99° to 103.5°, accompanied by distress in the lower abdomen. Examination brought out the following facts:

The patient was a well-developed middle-aged man. His complexion was muddy, his tongue coated, and his breath foul. Examinations of the heart, nervous system, and lungs were negative except for the rapidity of the heart and for signs of retraction at the left apex. The abdomen was uniformly distended and tympanitic. There was diffuse tenderness below the umbilicus, which was best defined in the left iliac fossa, and in the median line, where he always referred his pain. No tumor mass could be demonstrated. A slight visceromotor reflex was present in both lower quadrants, but was most marked on the left. There was no area of cutaneous hyperesthesia. Neither testicle was tender. Rectal examination was negative. The leukocyte count was 15,000. The urine contained much indican, but was otherwise negative. The stools were very offensive, contained a little mucus, but neither blood nor pus. Large thick Gram-positive bacilli were present in large numbers. The pulse was rapid (100 to 130).

With colonic irrigation and on a diet of buttermilk and carbohydrates the patient slowly improved. For a month there were occasional attacks of pain, with a little temperature, which were relieved by flushings. Convalescence was slow. Several leukocyte

counts during this period gave an average of 8000 to 10,000. Indican was more or less constantly present until convalescence was well established. A diagnosis of intestinal toxemia with possible sigmoiditis was made at that time.

The patient left home and did fairly well for one month, when he was taken with sudden, severe pain in the hypogastrium, hurried to the hospital, and was operated upon with the diagnosis of appendicitis. In a personal communication, the surgeon stated that "the appendix was thickened and slightly injected, but I must confess it hardly seemed sufficiently involved to account for the large amount of turbid fluid which we found in the lower abdomen. There were no adhesions about the cecum, which was apparently normal. I did not examine the sigmoid colon."

One month later the patient returned for treatment. His distress had returned after the operation, although not to the same degree. A strict dietetic and hygienic régime with colonic flushing gradually brought the patient into the best health he had enjoyed for several years. Strict injunctions against excessive indulgence in proteids, especially high meats and cheeses, were given, as experience had proved that a minimum of proteid was accompanied with less distress. With much proteid ingestion, indican always appeared in the urine and undigested meat fibers in the stools. When the diet was strictly followed, the stools lost their offensiveness, the gas diminished, and the number of Gram-positive bacilli decreased. Repeated rectal examinations were negative.

After three months of comparative freedom from trouble, the patient committed two dietetic indiscretions within twenty-four hours. Pain and distress in the hypogastrium followed, with temperature ranging from 99° to 104°, and a pulse of 100 to 120. His condition improved slowly for five days under treatment, when a sudden sharp pain followed an injection of water. The pain was so severe that morphine was given before the patient was seen. On examination there was considerable tenderness in the lower abdomen, some rigidity, but no cutaneous hyperesthesia. Rectal examination was negative. There was a little nausea, but no vomiting. A tumor mass could not be demonstrated at this time; there was some pain at the end of urination. On several occasions during the next few days the stools showed a little pus, mucus, and blood. Ten days later a mass had clearly defined itself in both iliac fossa, and could be detected per rectum as an irregular, elastic, bulging body. The patient's general appearance was decidedly septic, and he was removed to the hospital for operation. Leukocytes, 40,000.

From the clinical course it was assumed that the condition was a localized purulent peritonitis rising from the sigmoid. A chronic ulcerative process was excluded on account of the absence of blood and pus in the stools until the last few days. Perforation of a carcinoma was unlikely from the length of the clinical course

absence of blood, the absence of a tumor until a few days previous, (two years), the absence of signs of stenosis, the almost entire the character of the tumor, and its rapid development. By exclusion, diverticulitis of the sigmoid with the perforation of an infected diverticulum resulting in a pelvic abscess was considered probable.

Operation. An incision was made in the median line, and inasmuch as the most prominent part of the tumor mass seemed to the surgeon to be on the right side, a wide incision was made well to the right of the rectus muscle, and free drainage instituted. The case passed from observation, and death took place about six weeks after the operation. The autopsy report was as follows:

Operation about ten hours after death. Skin very pale. Slight rigor mortis. Peripheral lymph glands not enlarged. Two operative wounds on abdomen—one in mid-line about 10 cm. long; one over appendix about 7.5 cm. long. The latter drained. Subcutaneous fat well developed.

Upon opening the peritoneal cavity it was seen that the omentum was adherent over the whole anterior surface of the peritoneum, and less extensively to the intestinal coils. It was rolled into a mass in the left hypochondrium.

The intestinal coils were more or less generally adherent by old fibrous adhesions, and were also adherent to the parietal peritoneum in the right flank. The coils of the ileum were closely adherent to one another, and the lower ones were also adherent to the sigmoid by old and recent adhesions.

The cecum was bound down by adhesions, most of them recent, the results of an operation done some days before to drain the cecal and pelvic regions. There was no pus in the pelvis or about the cecum. The appendix had been removed.

The intestines were carefully dissected out and no other process than an adhesive fibrosis was encountered until the lower loops of the small intestines were dissected away from the sigmoid, just at the brim of the pelvis. At this point an abscess cavity situated under the sigmoid and walled off by the small intestine was opened.

As the large intestine was removed, pus was again encountered to the left and beneath the descending colon and sigmoid. This suppurative process could be traced to the abscess cavity mentioned above and to a larger one to the left of it, in the postintestinal tissues and just at the brim of the pelvis. The process had apparently also extended down (judging from the adhesions), but this extension had been limited by adhesions in the pelvis. Extending up along and behind the descending colon the line of extension of suppuration could be followed to the spleen, which was half enclosed in an abscess cavity.

An incision through the diaphragm from below and exploration of the left pleural cavity occasioned a gush of foul-smelling, greenish-yellow, thin pus to the amount of about 500 c.c.

The thorax was then opened and examined. The left lung was partially compressed by an empyema that extended from the diaphragm to near the apex. The pleura was covered by a greenish-yellow fibrinopurulent exudate. The left apex was the seat of a large healed scar, and scattered about on the pleura and in the pulmonary tissue were fibroid and calcareous obsolescent tubercles.

The right lung was also the seat of a healed tuberculous process, the pleura being thickly studded with obsolescent tubercles, especially at the junction, posteriorly, of the interlobar clefts.

The heart was pale but otherwise normal.

The liver was small, pale, and exceedingly soft.

The kidneys were very large and pale. The capsules stripped, leaving an untorn surface. Section of the organ showed the cortex enlarged, pale, and granular in appearance, with little line of demarcation between it and the medulla.

The adrenals were normal.

The pancreas was normal.

The spleen was of normal size, but soft, and the seat of an acute suppurative perisplenitis.

When the intestines were opened it was seen that the small intestine was atrophic, the walls thinned, the rugæ not prominent, and the mucosa thinned. From the cecum down, the submucosa and the muscularis became gradually thickened until, in the vicinity of the brim of the pelvis, the wall was from two to five millimeters thick, and perisigmoidal and rectal tissues were generally firm and infiltrated.

The sigmoid and rectum showed accentuated diverticular pouches, all of which had thinned distal ends and mouths about which the submucosa and the muscularis were very thick and edematous (Fig. 4). Extending from the distal end of one of these pouches was a sinus, surrounded by thickened fibroid walls, that communicated with the larger postcolonic abscess cavity. From this pouch or diverticulum the suppurative process had apparently originated. The tops of the folds of the descending colon and sigmoid showed numbers of small areas having somewhat the appearance of shallow ulcers. These areas measured not more than one by two millimeters. They had slightly thickened, raised, and rounded margins, and gray bases.

Anatomical Diagnosis. Anemia; catarrhal sigmoiditis and proctitis; diverticulum formation; chronic perforative diverticulitis; suppurative perisigmoiditis, pericolitis and perisplenitis; empyema; parenchymatous degeneration of the kidneys; fatty degeneration of the liver; obsolescent, calcareous pulmonary tuberculosis; left apical scar; general organized peritoneal adhesions; operative wounds.

The striking clinical features of this case are the absence of constipation, the indefiniteness of the bowel disturbance, the repeated

presence of large quantities of indican in the urine, the unfavorable influence of a proteid diet, the persistent rapidity of the pulse in all of his attacks, the distress at the end of urination, the fact that perforation evidently followed distention of the sigmoid with water, the fact that a surgeon of high diagnostic ability operated for what seemed to be an acute attack of appendicitis, the interesting distri-

FIG. 4.—Photograph of the sigmoid of Case I, to show the site of the perforated diverticulum and the mouths of other small ones (*X*).

bution of the tumor mass, which extended from the left iliac fossa down into the *cul-de-sac* and up into the right iliac fossa, where it reached its greatest prominence, and that this led a surgeon of large experience, after making a median exploratory incision, to drain the apex of the abscess in the right iliac fossa, with the belief that the seat of the trouble was there.

Case II.—The following case was seen with Dr. Schleier, of Omaha. J. S., male, aged eighty-three years. The patient entered St. Joseph's Hospital December 9, 1908, in a semicomatose condition. No history could be obtained except that three days before admission he had had some trouble in passing urine and had, therefore, been catheterized. Subsequent urination had been free and the urine bloody.

General examination proved negative, except for a pulmonary emphysema and a well-developed arteriosclerosis. The abdomen was distended. Peristaltic waves could be seen starting in the region of the cecum, disappearing in the right hypochondrium, and again appearing at the median line, thence proceeding to the left and downward to the hypogastrium. There was no abdominal rigidity. There was tenderness posteriorly over both kidneys, with an area of renal hyperesthesia on both sides above the crest of the ilium. There was no abdominal tenderness. The bedsheets were stained with bloody urine; a specimen could not be obtained by catheterization. The breath was not urinous.

Rectal Examination. The rectum was ballooned, the prostate moderately enlarged, but not tender. No tumor mass was palpable.

Clinical Diagnosis. Chronic intestinal obstruction, probably due to stricture, cause unknown. Without a urine examination a chronic intestinal toxemia was suggested as a possible cause of the hematuria. Colotomy was advised and performed by Dr. Schleier. Death occurred about eighteen hours after operation.

Autopsy was performed eight hours after death. The patient was a somewhat emaciated elderly man. There was moderate edema and posterior congestion of both lungs, and marked senile emphysema. The heart was normal in size; there was tremendous calcification of the mitral valves and complete calcification of certain areas in the coronary arteries; there was also calcification of the aortic valves, and marked atheroma of the aorta throughout its entire length. The celiac axis was almost completely obliterated. The large intestine was dilated throughout its entire length; the hepatic flexure was adherent beneath and covered by the liver, a condition which explains why peristalsis could not be seen in this region. A colotomy wound was observed at lower part of descending colon. There was a stricture at the junction of the middle and lower third of the sigmoid. Numerous false diverticula were present in the area of the stricture, which was about one and one-half inches long (Fig. 5). There was a slight perisigmoiditis at the site of the stricture. Diverticula were numerous for a distance of a foot or two above the stricture. They varied in depth; their mouths were generally wide, and they entered the appendices epiploicæ. There was atrophy of the walls of the colon and of the small intestine. The kidneys were normal in size, the capsules stripped easily, and the surface was slightly granular. The cortex was atrophic, but there

were no gross signs of inflammation. The pelvis and both kidneys were markedly injected and covered with a dirty, sanguinopurulent exudate. The ureters were distended and similarly inflamed. They were so red and injected as to look like veins from the outside. The bladder wall was thickened and markedly injected. The bladder contained a small amount of bloody urine which showed pus cells and desquamated epithelium in large amounts. There were microscopic clumps of a dozen or more epithelial cells together,

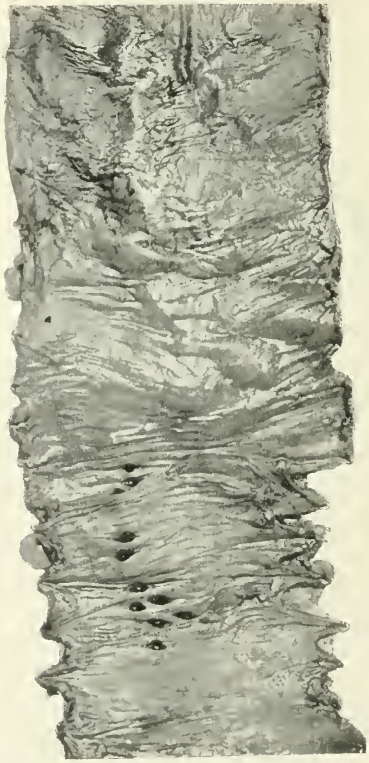


FIG. 5.—Photograph of the sigmoid of Case II, to show diverticula in the portion involved in the stricture.

showing that desquamation *en bloc* of areas of bladder, ureteral, and pelvic epithelium had occurred. The prostate was hypertrophied; there was marked peripheral arteriosclerosis, with extensive deposits of lime salts in the vessel walls. The pathological diagnosis was emphysema and passive congestion of the lungs; coronary arteriosclerosis and calcareous deposits in mitral and aortic valves; general arteriosclerosis; passive congestion of liver and spleen; senile atrophy of spleen; chronic intestinal obstruction

due to benign cicatricial stenosis of sigmoid; false diverticula of the descending colon and sigmoid, especially at area of stricture; dilatation and atrophy of the colon; hypertrophy of the prostate; ascending cysto-uretero-pyelitis.

The intimate relation of the numerous false diverticula to the stenosed areas in this case makes probable their pathogenic significance in benign cicatricial stenosis of the sigmoid.

Case III—S. B., farmer, aged fifty years, entered St. Joseph's Hospital January 4, 1909. The patient was in a stuporous condition, and the following history was obtained with difficulty. The duration of illness was indefinite and onset had been gradual. The patient complained of intermittent abdominal pain, which was described as "sore, colicky," of belching, headache, weakness, and of constipation. His bowels had not moved at all for three days, and not well for several weeks previously. No pulmonary, cardiac, or renal symptoms could be elicited. The past history was negative except for indefinite trouble with the lower bowel, and constipation. Later, a history was obtained of a disturbance, nine months previous, in the lower abdomen, which lasted several weeks, and was characterized by colicky pains and distress in the median line and to the left, alternating diarrhea and constipation with mucus in the stools, fever, and soreness in the left lower quadrant. The condition of the patient when first seen was as follows. He was an emaciated, medium-sized man, stupid in appearance, and apparently of some sixty years of age. He lay quietly in bed, yawned continuously, his eyes were half closed, and he paid but little attention to what was going on around him. It was necessary to speak loudly and prod him to obtain answers to questions. Both lids were equally ptotic, but he could raise them with the assistance of the frontal muscles to the level of the iris. The pupils were equally contracted, and reacted slightly to light and distance. The breath was foul, and the teeth poor. Vision seemed good. There was no asymmetry in muscle power. The patient could recognize a watch tick for a distance of only about an inch from each ear. Examination of the neck, lungs, and heart was negative. The abdomen was soft and not especially tympanitic. The liver and spleen were negative. Peristaltic waves occasionally could be seen traversing the hypogastric region from right to left. They were about two to three inches in breadth and were accompanied by signs of distress and rubbing of the abdomen. Rectal examination, save for "ballooning" was negative. No tumor mass was palpable. The urine was highly concentrated. It contained indican and urobilinogen (Ehrlich's aldehyde reaction) in large amounts, a trace of albumin with occasional hyalin, and granular casts. The superficial reflexes were markedly diminished, and the deep reflexes were faint or absent, but symmetrically so. The temperature was 101°, and the pulse 70. An injection of warm olive oil was ordered, with a

mercurial and saline, which brought away a large amount of fecal material. The mental condition brightened for several days. Then relapses occurred at varying intervals with conditions similar to those described. The trouble always could be relieved by a rectal injection of one to two quarts of water. A diagnosis of chronic intestinal obstruction, of unknown cause, in the region of the sigmoid, was made at this time. On January 25, 1909, the patient developed a double lobar pneumonia, which lasted ten days. During this time injections of water were given each day.

On February 28, 1909, another attack of pneumonia occurred which produced stupor and was accompanied by signs of intestinal obstruction, *e. g.*, peristalsis and obstipation, which were relieved only by repeated injections of both oil and water. A large sacral decubitus four inches in diameter developed at this time. Several attacks of obstruction followed, which were easily remedied by injections. During intervals of from one week to ten days the patient had normal although constipated stools.

It was clear that an intermittent intestinal obstruction existed. This must have been caused by a mechanical factor prevailing only at intervals. The occasional copious and well-formed movements spoke against stricture. The constant absence of blood in the stools, and of a tumor mass, spoke against malignant disease. There was no evidence of hernia. Of causes that could produce such a frequent recurrence of obstruction, followed by free intervals, only two could well be assumed. The first was adhesions. But a band could hardly produce this picture by mere constriction. Traction of an adhesion on a loop of intestine might cause kinking when influenced by changes in intra-intestinal pressure, and by variations in the position and caliber of the gut, both of which factors are, to a certain extent, dependent on the intestinal contents. The second possible cause was intermittent volvulus upon the basis of cicatrization and retraction of the mesosigmoid forming an axis on which rotation of the sigmoid might occur. Such a condition might have accounted for an intermittent intestinal obstruction, which was not relieved by catharsis, but by rectal injections. A history of intermittent intestinal trouble with fever, pain, and diarrhea, with the presence of blood the year before, suggested the possibility of such a condition.

Operation was advised on the basis of a diagnosis of intermittent chronic intestinal obstruction, due to volvulus or to adhesions. An old inflammatory process resulting from a diverticulitis was suggested as a possible *causa morbi*.

The operation was performed by Dr. C. C. Allison. An incision was made to the left of the median line. The upper and lower segments of the sigmoid were found separated by about one inch of scarred mesosigmoid. There were slight adhesions running from the origin of the sigmoid to the parietal peritoneum. Several

diverticula were seen close to the mesenteric attachment in the vicinity of the retracted mesosigmoid. It could not be demonstrated without opening the gut, that the cicatrization was secondary to a diverticulitis, and so, although the existence of the diverticula may have been a coincidence, yet inference to the contrary is permissible. The upper limb of the sigmoid was freed from adhesions and stitched to the parietal peritoneum higher up. A complete recovery took place.

Case IV.—N. A. C., male, aged seventy-five years. The case was a coroner's autopsy. The anatomical diagnosis was: Myomalacia cordis; sclerosis and obliteration of the right coronary artery; general arteriosclerosis; passive congestion of liver, spleen, and kidneys; chronic interstitial nephritis; pulmonary emphysema. Several false diverticula of the sigmoid were found entering the appendices epiploicæ.

Case V.—E. R., male, the anatomical diagnosis was: Healed tuberculosis of both apices; chronic bilateral pleural adhesions; dilatation and hypertrophy of the heart; myomalacia cordis with cardiac aneurysm; passive congestion of lungs, liver, kidney, and

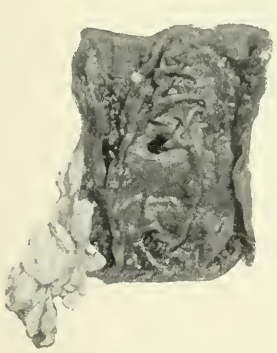


Fig. 6

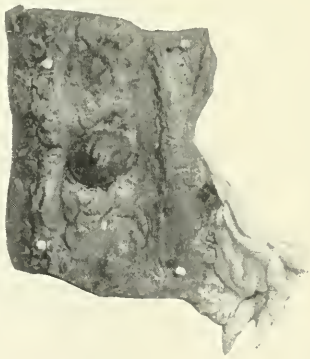


Fig. 7

Fig. 6.—Photograph of one of the diverticula in the sigmoid of Case V.

Fig. 7.—Photograph of the same diverticulum in Case V, showing the inspissated feces contained in it.

spleen; cholelithiasis; arteriosclerotic kidney; diverticula of the sigmoid and descending colon. The diverticula were located in the vicinity of the mesenteric attachment. Their walls were extremely thin, and they contained inspissated feces (Figs. 6 and 7).

Case VI.—The case was a coroner's autopsy. The subject was an elderly obese male, of unknown age. The anatomical diagnosis was: Edema of lower extremities; passive congestion and edema of the lungs; hypertrophy and dilatation of the heart, especially of the left ventricle; degeneration of the myocardium; passive congestion of the liver, spleen, and kidneys; chronic interstitial

nephritis; false diverticula of the sigmoid. The sigmoid was surrounded with a large amount of fat, and the appendices epiploicæ consisted of large fatty masses. Six false diverticula could be seen penetrating these fatty masses (Fig. 8).

Fig. 8.—Photograph of a portion of the sigmoid of Case VI, to show diverticula.

Diagnosis. It can be easily seen, from the brief *resume* of the pathology of diverticulum disease, that the symptoms may be manifold and difficult of interpretation. The diagnosis is seldom easy, rarely certain, and often impossible. Franke was able to collect from the literature only 2 cases in which the diagnosis had been made. To these he added a case of his own. Graham recently suggested the diagnosis in one of Mayo's cases. To appreciate the possibilities is a long step in the direction of a diagnosis, which must be made largely by exclusion. The most easily recognizable condition is that of the so-called "left-sided appendicitis." There is pain, gastric disturbances, tenderness, and rigidity in the left lower quadrant, with temperature and leukocytosis; abscess formation often appears later. Another class of cases that is moderately

easy of recognition is that of chronic hyperplastic sigmoiditis. This has been treated as a disease entity by Ewald, Boaz, Rosenheim, and others, but it is possible that diverticulitis may be found a basis for it. In this complex there is always intermittent pain, disturbed function associated with irregularity of bowel action, gas, and often spastic stools in which there is frequently an increase in mucus and occasionally a trace of blood. Physical examination discloses a tender sausage-shaped tumor which may be either adherent or freely movable, and which varies in size from time to time. Infiltration may be felt occasionally per rectum. Sigmoidoscopy shows a swollen, reddened, rugous mucosa, and often narrowing of the lumen of the gut. Obstructive symptoms may be present, but are not so common as in cancer, from which condition it must be differentiated. In carcinoma the clinical course is more progressive and definite. Its duration is limited; ulceration with blood in the feces is the rule, and when blood once appears it is usually quite constant. The tumor is harder, more likely to be movable, definitely circumscribed, constantly increases in size, and is not elongated. Bladder symptoms are apt to be frequent in diverticulitis, as the bladder is often involved in the inflammatory process. Cripps states that vesicosigmoidal fistula is more commonly inflammatory than malignant (45 out of 63 cases). If such be the case, many of them may be the result of a diverticulitis. Disturbed bowel function is constant. Many cases record constipation as a more or less pronounced prodromal symptom. Pelvic abscess, tuboövarian abscess, mucous colitis, amebic colitis, chronic proctitis, tuberculosis and syphilis of the sigmoid, psoas disease, retroperitoneal abscess in the left flank from other causes, etc., must, in addition to the conditions already mentioned, be differentiated.

Treatment.—The treatment must be surgical in many cases. The prognosis is often a question of technical efficiency. It is certain that, as in appendicitis, many of the cases will recover without operative interference. Just what are the indications for resection in hyperplastic sigmoiditis is a question for future determination. Abscesses and vesicosigmoidal fistulæ should always have the advantage of surgical treatment. As knowledge of the morbid anatomy of false diverticula increases, as cases are recognized, reported, and treated, as methods of surgical procedure become crystallized, facts will be obtained for reliable diagnosis and prognosis.

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PERFORATING ULCER OF THE DUODENUM: DEATH FROM PULMONARY THROMBUS.[1]

By Geo. Tully Vaughan, M.D.,

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This patient, a young man, aged twenty-nine years, was sent to me by Dr. W. C. Ford, of Woodstock. He gave the following history: For some years he had suffered at times with pain in the stomach, and what he called "indigestion." Two days before his admission to Georgetown University Hospital he was taken in the morning with griping in the bowels, which was relieved by going to stool. About 5 P.M., of the same day he was suddenly taken with severe pain in the abdomen, chiefly in the epigastrium, but extending below the level of the navel and upward on the right side to the chest and shoulder. He vomited several times a prune-juice looking material, and later on, still darker colored material. No chills.

On admission to hospital, forty-eight hours later, his pulse was 130, temperature 99°, abdomen slightly swollen, tympanitic, rigid, and tender, especially over the gall-bladder region, slightly over the appendix. In making the diagnosis the following conditions were considered in the order of probability: Perforating ulcer of the stomach, bowel, or gall-bladder, or appendicitis, and immediate operation was advised and was done. The incision was made through the right rectus muscle, and the region of the appendix was examined and exonerated. On passing the fingers upward, adhesions were felt and a turbid greenish fluid began to escape. The incision was prolonged upward, and a patch of lymph was seen on the anterior surface of the pylorus and first portion of the duodenum, with a hole about $\frac{1}{5}$ of an inch (1 cm.) in diameter in the centre of it, leading into the bowel, it was thought, from which the greenish-colored fluid was escaping. It was closed at once with fine silk sutures. Plastic lymph was found on the gall-bladder, liver, stomach, intestines, and anterior abdominal wall—extensive peritonitis existing and an abscess containing thick pus was found behind and below the right lobe of the liver. A rubber drainage tube wrapped in iodoform gauze was placed in the abscess cavity; the abdomen was wiped out with gauze, and closed around the drainage tube. Pulse 140 during and at the close of the operation. Salt solution by rectum, six ounces every hour, was ordered. From this time the patient steadily improved, and at the end of the seventh day his pulse and temperature were normal, the tube was draining freely, and his general condition was satisfactory. On the tenth day

[1] Read at the Virginia Medical Society in Norfolk, Va., October, 1910.

the temperature in the evening rose to 101°, pulse to 100, but the patient slept pretty well. Next morning the temperature was 99°, pulse 90, and he said that he did not feel so well, had some pain in the right side, and preferred to lie on his back, as it hurt him to turn. No trouble with respiration. About 4 P.M., while using the bedpan after an enema, he suddenly complained of difficulty in breathing, pulse became very rapid, his face and chest became cyanotic, he insisted on being raised up, but in a few minutes fell back dead—the entire attack not lasting over fifteen minutes.

This result was unfortunate and disappointing to the physician and to the friends of the patient—to have him snatched from the jaws of death and still lose his life, as if a man rescued from drowning should be suddenly struck dead by lightning—it was most discouraging. The cause of his death could hardly have been anything else than a cardiac or pulmonary thrombus, and this was probably caused by the infection of the abdominal cavity.

Pulmonary thrombus or embolism is said to be not very common. Albanus found that it followed 2 per cent. of abdominal operations. It seems to be more common after gynecological than general surgical laparotomies. Burkhard gives in 236 operations for uterine fibroids 12 cases of embolism (Keen's *Surgery*). While pulmonary and other forms of embolism are usually preceded by some kind of an infection, yet there are many cases in which the infection is not recognized or does not exist. Rough handling, bruising of the veins, has been given as a cause for embolism. I have seen many cases of embolism or thrombosis of the iliac and femoral veins following removal of the appendix, of the uterus, and other surgical operations in the abdomen, but I have seen only three cases of pulmonary embolism, and two of them were fatal. The first occurred in a boy, aged fourteen years, suffering from an infected gunshot wound of the knee-joint, the ball lodging in the joint, from which it was removed by incision. The symptoms came on five days after the receipt of the wound, although he had vomited the day before, and rested poorly that night. On the morning of the fifth day his pulse was 80, but very feeble, heart sounds almost imperceptible, skin cyanotic and cool all over body, no dyspnea, perfectly rational, and contented. Death occurred suddenly about half an hour after these symptoms appeared. The absence of distressing symptoms was probably due to the slow formation of the thrombus and the gradual arrest of the circulation.

The other case occurred in a woman, aged thirty-eight years, after an operation for double hernia. No infection existed so far as known, although the pulse ranged from 90 to 100 and temperature from 99° to 100°; but on the ninth day after operation the patient was taken suddenly with pain under the left breast, a feeling of oppression and difficulty in breathing, the pulse rose to 120, the heart sounds were weak and somewhat muffled, she had chilly

sensations, and vomited once. Nothing of note was heard over the lungs. These symptoms continued for about twenty-four hours, then gradually subsided, so that at the end of forty-eight hours the pulse. temperature, and general condition were nearly normal and recovery followed. In this case the embolus was probably small and was soon disposed of.

The treatment of thrombosis obviously consists in preventing infection and avoiding injury to vessels by rough handling during operations. The efficiency of the treatment by frequent change of position and short stay in bed after operations, in preventing thrombosis is still open to question.

A few surgeons have operated, opening the pulmonary artery and drawing out the thrombus, but so far without permanent success. Sievers and Trendelenburg, of Leipzig, have each operated on a case. Trendelenburg opened the pulmonary artery and removed a thrombus thirteen inches long, but the patient died thirty-seven hours later.

PURPURA HÆMORRHAGICA, WITH REPORT OF AN ATYPICAL CASE.

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AND

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Purpura is often looked upon as a disease, especially in that form known as the idiopathic variety, but it is not at all improbable that if the exact etiological factor in the so-called primary or idiopathic cases could be determined, we would have to consider this trouble as a symptom, rather than a disease. Although purpura has been carefully studied for many years by careful observers, we know very little of a definite nature about the causation of the primary cases. Dr. Osler has referred to purpura as "that obscure and interesting manifestation of which we know so much and at the same time so little." Histologically purpura used to be confused with the contagious fevers, especially the eruptions of scarlet fever and measles. It was not until the latter part of the seventeenth century that a clear description of this disease was given by Zeller. Before proceeding farther, it should be stated that the case to be reported belongs to the primary or so-called idiopathic purpura, which is not to be confused with the more ordinary type of secondary purpura occurring in such troubles as typhoid fever, nephritis, heart disease, lymphatic leukemia, pneumonia, arteriosclerosis,

alcoholic neuritis, cachectic states, as senility, iodine idiosyncrasies, and many others.

Divisions and Frequency. It has been customary to divide idiopathic purpura into the mild, moderate, and severe grades, or purpura simplex, purpura rheumatica, and purpura hæmorrhagica. These types are frequently not sharply defined. That idiopathic purpura is a rare condition is shown by statistics.[1] At the Massachusetts General Hospital there were only 65 cases of idiopathic purpura among 155,884 patients during a certain period. At the Johns Hopkins Hospital, 41 cases were observed in 18,594 medical patients. At the Hamburg General Hospital there were 73 cases in forty-one years in a total of 100,000 patients. Some authorities believe the affection is not uncommon, but in such instances it is very probable that both the secondary and idiopathic forms are grouped together under one heading. Stelwagon states that the disease is not uncommon, then he proceeds under the heading of causal factors to mention such conditions as malaria, grip, profound anemia, syphilis, nephritis, etc., clearly showing that he has joined the two types under the common term purpura.

History of the Case. The patient was an insane male, a case of dementia præcox, aged thirty-five years, whose physical condition previous to the onset of the trouble was at par so far as known, aside from an anemic appearance. During the night of June 21 he was taken suddenly ill with nausea and vomiting. There were two attacks. The vomitus contained nothing characteristic. There were a few food particles and much mucus at first, and the second vomitus consisted of a watery fluid, with some mucus. The following morning he ate no breakfast, but took some nourishment for dinner and supper. An examination of his physical condition revealed nothing abnormal. His stomach was not sensitive; bowels were regular; pulse and temperature normal. He complained of feeling a little weak in the morning. As he appeared to be in his usual health during the afternoon, he was allowed to dress and go about the ward. The following night he was again taken with three vomiting spells. He refused breakfast. There was no fever; pulse, 90. Examination showed some general tenderness over the stomach, which was produced probably by frequent retching. The patient was kept in bed, and showed no additional symptoms until the morning of June 24, when a profuse hemorrhage occurred from the bowels. Vomiting began immediately, and in the vomitus were observed brownish streaks (decomposed blood). The cause of the hemorrhage could not be ascertained. Leukemia, hemophilia, and purpura hæmorrhagica were considered. The blood examination eliminated leukemia. Hemophilia was discarded by a negative family history, a normal blood-clotting time,

[1] Osler's Modern Medicine.

the male sex, and development after puberty. For purpura hæmorrhagica there were no skin lesions.

The patient failed rapidly. During the following two weeks there was rapid emaciation, due to frequent and profuse hemorrhages from the bowels and stomach and inability to retain nourishment. Temperature was never above 100° F. Rectal feeding could not be resorted to, owing to his violent and resistive tendencies. Medicinal measures did not relieve the nausea, vomiting, and hemorrhages. Signs of collapse were apparent. Pallor was marked; expression anxious; temperature subnormal, with cold, perspiring skin; thready pulse, and great emaciation. July 6, while in this condition, there were presented the first signs which gave a clue to the affection we were dealing with. There appeared upon the extremities about the elbow- and knee-joints a few petechiæ, varying in size from a pin-point to an eighth of an inch in diameter. These gradually increased in number during the next few days, until there were two or three dozen spots on each extremity. Later, a few spots occurred upon the trunk. Now and then a small hematoma was seen. With the development of the skin lesions and the administration of special medicinal measures the constitutional symptoms began to abate. From this time on there was a slow, but steady improvement.

The interesting and unusual circumstance connected with this case is the fact that there were no evidences of any integumentary lesions until the constitutional symptoms had practically run their course and had almost caused a fatal termination. In the treatises on purpura to which I have had access, no mention is made of this peculiar course, but Osler's *Modern Medicine* speaks of purpura hæmorrhagica without skin lesions. To quote: "There are some cases of the hemorrhagic diathesis which present the clinical picture of purpura hæmorrhagica, except that cutaneous hemorrhages are absent. There is no hereditary or congenital tendency to hemorrhage, and hence they cannot be classed under hemophilia. In some chronic cases of this type the diagnosis is confirmed subsequently by the appearance of purpuric spots in the skin." Osler[2] has reported such a case, with recurring abdominal crises and bleeding at the nose for a year, before a purpuric rash appeared during an attack. J. W. Coe studied a patient in whom during a period of twenty-eight years there had been frequent attacks of epistaxis so severe that packing of the nostrils was often necessary. There was no history of bleeders in the family, and the subject had never had arthritis. Owen observed a case of this type in a girl, aged eleven years, who had hemorrhages for twelve months, first from the bowels, then the nostrils, and afterward from the

[2] Amer. Jour. Med. Sci., December, 1895.

left ear. There was no history of bleeders in her family, no arthritis, and no purpura.

Etiology. The exact cause of true or primary purpura and its mode of production are unknown. Symptomatic purpura may occur in many conditions, as I have already mentioned, but in the disease purpura the hemorrhagic tendency is not congenital or hereditary, in contrast to hemophilia. It is met with in both sexes and in all ages, but is most frequent in the second decade, and rare after fifty years. No one cause can at present be set down as essential in all cases. Microörganisms have been looked upon as causative in many of the more grave cases. At least three experimenters have succeeded in producing the malady by inoculating animals with pure cultures. Stelwagon believes that the causative factors may be divided, in general, into vasomotor, toxic, and infectious, but he includes the secondary with the idiopathic cases. In the case I have reported the symptoms would seem to indicate a toxicity of the intestinal tract, but whether this was an auto-intoxication starting from the intestinal tract or due to a toxic condition of the blood with elimination of certain poisonous products into the stomach and bowels can only be conjectured. The patient's anemic appearance might have suggested a deficiency in the hemoglobin and number of red cells as a possible etiological factor, but any anemic blood condition which might have existed prior to the onset of the trouble could not have been very pronounced, for after several large hemorrhages had occurred, the red blood cells numbered 3,300,000 per cubic millimeter.

Pathogenesis. In considering the pathogenesis of purpura, we must necessarily turn our attention to the study of the condition of the blood and bloodvessels. As the question is still unsettled, it would seem important to give a few of the more recent views concerning its production and the changes accompanying it. It is certainly well established now that the bloodvessels are concerned in the production of purpura, yet the changes in the vessels may be induced secondarily by the alterations in the blood composition. The changes found in the bloodvessels at autopsy are not constant. Riehl describes the presence of localized degeneration of the vessels in all cases of purpura. Adami, in his recent work on *Pathology*, speaks of a fatty hyaline degeneration occurring in the walls of the smaller vessels in all cases except the neuropathic variety. Von Kogerer claims that a careful search would always reveal the presence of thrombi due to vascular degeneration. According to this theory the disease of the vessels leads to thrombosis and this in turn leads to the hemorrhages. The way by which the blood cells leave the vessels is not known. Many pathologists have examined the purpuric spots without finding any breaks in the vascular walls. Clinicians object to the theory of primary vascular degeneration, for it is difficult to see how the hemorrhages can be so widespread

over the surface of the body and develop with such rapidity. Also the tendency to hemorrhage is transitory, and one cannot readily conceive of so severe a disease of the bloodvessels being such a transient affair. Flexner discovered a substance in snake venom which when injected in laboratory animals possessed the property of destroying endothelium and producing multiple hemorrhages in a few minutes. Gay and Southard also report experiments in which the lining epithelium of the capillaries was so changed that focal hemorrhages occurred in as short a time as four minutes. These experiments certainly suggest the possibility that in purpura there is a substance present in the blood which produces an endotheliolysis with focal hemorrhages.

We will now discuss briefly the changes that occur in the blood itself in purpura. Dennes, a Belgium pathologist, and Hayem, in 1890, noticed the marked diminution of blood platelets in purpura. Recent investigators have confirmed these findings, and even say that it is characteristic. Normally, the platelets number from 200,000 to 600,000 per cubic millimeter. In purpura they range from 10,000 to 42,000 or higher, but in practically all cases they are markedly diminished. Hayem has described another change in the blood in purpura. Normally, the blood clot quickly contracts and expresses serum. The clot in purpura hæmorrhagica does not retract, and there is no extrusion of serum. Others have confirmed this finding, and experiments have been performed to ascertain the behavior of blood from which the platelets have been removed. It was found that when the platelets were filtered out the blood clotted slowly, and the clot did not contract and no serum appeared. It seems quite natural, therefore, to ascribe the contraction of the clot with expression of serum to the presence of the blood platelets which we find so diminished in purpura hæmorrhagica. Albumose injected into the circulation of animals diminishes the number of platelets, and Hayem produced a condition analogous to purpura by injecting the serum of an animal of another species. The platelets collected in masses forming thrombi, leaving very few in the circulatory blood. He concludes that the diminution is due to their destruction, which may be brought about by the introduction of toxins from the digestive tract. This same view of auto-intoxication is also held by other prominent writers. It seems quite probable that in cachectic states, such as leukemia, nephritis, carcinoma, etc., with purpura that the toxic substances formed are likely to produce profound changes in the blood, which lead to rapid disintegration of the vessel walls or to the slower hyaline or fatty degeneration. This, however, is not the idiopathic variety. Undoubtedly there is a combination of factors at work in the production of purpura. As a basis of the condition we have a change in the composition of the blood causing a more or less marked disintegration of the lining epithelium of the vessels, which allows the blood to pass through

into the tissues giving the hemorrhagic spots. One of these very prominent alterations we have seen in the marked diminution of the blood platelets. Whether this alteration is dependent upon an obscure infection or upon an autointoxication is problematic. It would be interesting to determine in cases of autointoxication if there is a diminution in the number of blood platelets, and if the blood clot lacks an inclination to contract quickly and to exude serum.

It is unfortunate that the case we have here reported was not worked up from the laboratory standpoint at the early part of the disease and later at the height of the process. The patient was well along in convalescence when the blood examination was made. There was a moderate anemia, the red cells numbering 3,300,000 per cubic millimeter. The leukocytes were practically normal, numbering 7300. This finding rather discourages the idea of infection in this case, unless we were too late to observe a leukocytosis. The blood platelets as we are led to expect were markedly diminished, numbering only 18,700 per cubic millimeter, instead of from 200,000 to 600,000 in the normal blood. We were unable to verify the non-contraction of the clot and failure to express serum, but we must consider that the case was far along in convalescence at the time of the examination. The urinary examination at the time of the patient's illness was negative aside from a large increase in indican which so often accompanies auto-intoxication.

Treatment. The successful treatment of any disease depends upon getting at the etiological factors. Of course, in secondary purpura we direct our attention to the conditions under which they arise. Whether or not we are dealing with the idiopathic or secondary forms, the patient should be kept in bed to insure absolute rest. The mildest types may not require this. Among the various agents used should be mentioned sulphuric acid, ergot, turpentine, gallic acid. Opinions vary as to their therapeutic value. Osler favors oil of turpentine in 10 to 15 mm. doses, three or four times a day. It is known to be a hemostatic, but owing to its irritating tendency and consequent liability to cause inflammation of the kidneys it should be used with care. Stelwagon has met with success in the grave forms with ergot given by subcutaneous injections. Adrenalin has been very beneficial in hemorrhages from the mouth and stomach. If used for intestinal hemorrhage it should be given hypodermically, as it is decomposed in the stomach. Owing to the persistent nausea and vomiting in our subject at the height of the trouble, nothing could be retained on the stomach, not even cracked ice. Wright has advised for the hemorrhages a trial of calcium chloride in 20-grain doses three times daily, basing its probable value upon its service in lessened blood coagulability, which from his investigations seemed to be the direct etiological factor. The remedy should not be given, however, for more than

several days, as its continued use finally diminishes the coagulability. Pratt, reporting in Osler's *Modern Medicine*, said that in some of their severe cases the use of calcium salts was of no benefit. On July 6 the case here reported was a very sick man. Vomiting continued, with occasional hemorrhages. This day he was placed upon 20-grain doses of calcium chloride, three times daily. From this time on recovery, though slow, was steady. There were no more nausea, vomiting, or hemorrhages. After four days he was given a rest from medication for three days, and then placed upon calcium lactate for one week. Tonics, a liberal diet, and iron aided the convalescence.

Just how much credit should be given the calcium chloride and lactate administered in this case cannot be stated with any degree of certainty. As before mentioned, Dr. Pratt has not met with success in using calcium chloride in some severe cases; others report more favorably.

We are very grateful to Dr. Chas. W. Pilgrim, superintendent of the Hudson River State Hospital, where this case was observed, for granting permission for its publication.

NEOPLASMS WITHIN THE SKULL: THEIR EARLY DIAGNOSIS AND SOLE TREATMENT.

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The treatment of intracranial tumors is at present in the same false position as was that of appendicitis fifteen years ago. At one time all cases, and even now most of them, die without receiving any real treatment; for the giving of potassium iodide is merely ritualistic. No case is recorded in which a postmortem has proved that a non-specific growth had been cured by drugs. As short of surgical removal, only death is to be expected, the term "expectant" applied to other treatment is a misnomer unless the expectancy refers to the patient's certain death. Temporary improvement, whether spontaneous or from narcotics or potassium iodide, does not justify postponement of the only real treatment. It would be as reasonable to postpone an appendectomy because of the comfort a victim might derive from opium.

Even in most of the cases which do come to operation, careful clinical investigation reveals an unequivocal history of intracranial disease, often of several years' duration. It is our duty to find out

and enunciate the earliest signs which point to intracranial neoplasms, in order that we may bring to the patient, before he is hopelessly moribund or permanently damaged, that relief which can be obtained in only one way. I refer to surgical removal of the growth.

This is my own firm opinion, but the words are a condensation of those of Sir Victor Horsley, delivered in October, 1910, to the German Society of Neurology at Berlin. I am the more impelled to quote them here because of the recalcitrance which I have encountered regarding my urgent advice to operate upon a number of cases about which I have been consulted in Washington. In no single instance has my advice been followed, and the patients have all died, with the exception of one seen only a few weeks ago, and of another of whom I have lost sight.

Before relating a few of these, it is good to emphasize the symptoms which should create suspicion of a cerebral tumor. Fine focal epilepsy is the most striking of these. Bravais-Jacksonian attacks are rarely due to other than local irritation. The diagnosis of epilepsy and the exhibition of bromides in such cases denotes an ignorance utterly injustifiable at this day. Such a case should be at once examined by someone versed in neurological technique. By refined measures of diagnosis, signs may be elicited by which an interpretation can be made, and a surgeon can then be called in at a time when a growth can be removed with certainty and without danger. The same remarks apply not only to focal epilepsy, but to any focal symptom at all. Thus, slowly progressive or recrudescent paralysis strongly indicates neoplasm, when granulomas are excluded. Slight losses of the attitude or muscle sense in one hand are similarly significant. So also is diminution of the other sensibilities. General or partial dystaxia or dysergia should always be investigated from this point of view. Slight differences or irritations of the special senses are the earliest symptoms of some cases. Aphasia of different types may be the first symptom. All these, in the early stages, have great focalizing significance. But it is not sufficiently realized that certain forms of mental dulness, of amnesia, of emotionalism, and changes in character are of localizing import as regards the destructive or irritative effects of a tumor of the frontal lobe.

Now, when one of these symptoms is found and a neoplasm is suspected it has been the procedure to wait for signs of cerebral compression before resorting to operation. The absurdity of this antediluvian attitude should need neither indication nor insistence, but that both are required is shown by my experience in Washington. An analogy will make it clear. Suppose that a surgeon, before removing a diseased appendix, were to wait for perforation, peritonitis, and abscess formation; does any one suppose that the mortality from appendicitis operations would be negligible, as at present? Would not such a diagnostician be a laughing stock? Again,

if the removal of carcinomata of the breast was always delayed until glandular involvement assured the diagnosis, would not their fatality approach 100 per cent? I doubt if the surgeon who awaited this kind of certainty of diagnosis would ever find a case to operate upon.

Now, the neoplasms found within the cranium are often benign, and none have the malignancy of mammary carcinoma. Moreover, many of them are diagnosticable, while very small, on account of the functional responsiveness of the tissue they invade. Hence their operability, technical difficulties apart, should be more hopeful than that of cancer of the breast, bowel, or uterus. Again, the subarachnoid sac is a less delicate structure than is the peritoneum, and the brain is less easily traumatized than are some of the structures of the abdomen. Hence the technical difficulties are largely mechanical, and, indeed, many of them are already overcome by the labors of Horsley, Krause, Cushing, and others.

Hence exploratory operations within the cranium are no more dangerous and no less justifiable than they are within the abdomen, always provided that sufficiently precise indications can be furnished the surgeon by the diagnostician. These are now available, and have been laid down by myself and others following such authorities as Bruns, Oppenheim, Duret, Horsley, Collier, Allan Starr, Mills, Spiller, Cushing, and others. It is only by their utilization that it is possible to detect an intracranial growth before an extensive destruction of tissue has occurred, and it is only then that an operation can be successful, in so far as complete restoration of function is concerned, and that is what should be aimed at by every physician. Even when the opportunity for intervention is too late to restore function, however, a proper operation can nearly always prolong or even save life.

The corollary of these propositions is that drug or expectant treatment is utterly unjustifiable, for the only eventuality to be expected from such measures is the patient's incapacity and death.

Case I.—A woman, aged about fifty years, seen with Dr. Gerry Morgan, who suspected some cerebral trouble because of his failure to prevent recurrent vomiting. There had been severe headache, staggering gait, and fainting spells. I found the woman in bed, somewhat dazed. Memory was much impaired, and she had to search for her words. There was no word deafness, nor aphasia, properly speaking, but incoherence had appeared now and then. I found a complete left lateral homonymous hemianopsia, but no contraction of the color fields other than this. The pupils reacted to light. There was marked edema of both optic papillæ. There was slight nystagmus with the lateral movement of the eyeballs. The attitude sense of the right hand was impaired. There was a right facial paresis, but no other motor loss. The gait was not cerebellar, and hardly uncertain. The plantar reflexes were in flexion. The

Achilles reflexes were diminished, the right being almost absent. The right patellar reflex was weaker than the left. The brachial reflexes were absent, as was the right abdominal reflex.

On account of the headaches, projectile vomiting, amnesia, difficulty of speech, and choking of the optic disks, I believed that there was a growth, and that it was in the right occipitotemporal region on account of the left lateral homonymous hemianopsia. I advised operation, to be preceded by a few days further observation and study to define the locality still more precisely. But the next day I was suddenly again called to the case. We found the woman curled upon the left side, stuporous, and vomiting. On examination, the plantar reflex was now in extension. The pupils were more contracted, but reacted fairly well. There was no further modification of sensibility, as far as could be found. We had taken with us Dr. Wellington, realizing in advance the need for urgent operation. After consultation, we advised removal to a hospital at once, and operation; but we did not decide whether to decompress in the subtemporal region or to uncover the presumed seat of the growth. However, the decision was never needed, for the family summoned a former attendant, who in turn called in two other consultants, whom he well knew would discountenance trephining, and the patient was allowed to die, which she did shortly afterward.

Case II.—Referred for opinion and care by Dr. Carl Henning. Complains of feelings in the head, "as if twisting around," for over three years. The vision has been much dimmed. She has had convulsions, which she cannot describe, severe frontal headaches, stiffness and pain at the top of neck behind, slight nausea, occasional dizziness. On examination, I found a commencing atrophy of the optic disk, with a swelling of about one dioptre. Great asthenia. An uncertain, staggering gait, not cerebellar in type. Great slowness of thought and speech, with incapacity to remember details clearly. No apraxia could be elicited. Rotation tests were negative. The deep reflexes were exaggerated, but plantar flexion was prompt and complete. The smell was defective in the left nostril, and the sound of the Weber tuning-fork test was lateralized to the left. No other sensory modifications could be ascertained.

Without observation or actual description of the convulsions, localization could not be precise; but that there is a growth present needs no argument, and that it is in a frontal lobe is to be presumed from the convulsions, obnubilation, the site of headache, the staggering gait not of cerebellar type, the negative rotation tests. The presumption that the growth is in the left frontal lobe would be rendered certain or not by the observation of one of the convulsions, and perhaps by a study of the nature of the amnesia.

The exploratory operation gives the certainty of great relief and the possibility of extirpation of this growth and cure of the patient. This was arranged for, but before it could be done the patient's

husband wrote that she was under other care, and that he did not desire it; and she has passed from observation.

Case III.—A woman, aged fifty-five years. The family physician relates that two or three years ago he diagnosticated "petit mal." During the attacks a cold sensation mounted the limbs of the left side and she fainted. She had dizzy attacks, headaches, false reminiscences, left hemiparesis, and weakness of memory. A year ago a consultant took charge of the case. He informs me that the unconscious attack lasted only a few seconds, and was not followed by dulness; that the left-sided paresis became worse and better by turns; that expulsive vomiting had been recurring for some time; that she was disorientated and confused, and that the pulse rate varied markedly. No diagnosis had been made.

The relation of these signs itself points most strongly to intracranial neoplasm, and an exploratory operation would have been justifiable upon them alone.

Sensibility. Upon examination I found an impairment of the attitude sense on the left arm and enlargement of the circles of Weber on both hands, forehead, and tongue. Hypesthesia to cold on left lower leg and toes. No marked impairment of vision or restriction nor inversion of fields, and no edema of the optic papillæ. Sometimes she confessed to smelling a hop-like odor in the mornings. The deep reflexes were all exaggerated; the abdominal reflexes were absent, and the left plantar was incomplete.

Motility. The motility was in general feeble, and her mental state prevented quantitative reliable tests. There was distinct facial asymmetry, the left side being weak. There was no strabismus, no nystagmus, nor inequality of pupils. The diadokokinesis was impaired, especially on the left side. The contralateral synergic response was diminished in the left lower limb. The attacks occur after a headache and a creeping numb feeling in the back of the neck, the arm, and leg, which lasts for a few days. No dyspraxia could be elicited.

Intelligence. Mental hebetude was distinct. For example, she called a quarter a nickel, although she disproved asteriognosis by declaring that she felt the milling on the edge. She was much disorientated, not even knowing the date or recognizing people she well knew.

The findings in this case leave no doubt of some slow invasion of the right frontal lobe. Its nature can only be determined by exploration. An operation for the purpose would at the same time relieve the patient, even though an irremovable growth were revealed. I so advised, but it has not been done on account of the timorousness of the physicians in charge of the case, whose failure to make a diagnosis for two years may be responsible for their own opposition to an operation now.

I could cite several other cases, but do not wish to prolong an

argument which should already be so clear as to admit of no misunderstanding, and the conclusion of which I may restate as the imperative necessity of an early neurological examination of any patient complaining of vague intracranial discomfort, symptoms loosely called neurasthenic or hysterical; progressive weakness; clumsiness or dulling of sensibility in any part of the body; nausea and dizziness; dimness of vision not due to refractive errors, especially if evanescent; peculiar subjective sensations of taste and smell; mental dulness; loss of memory or change of disposition. It is only by this means that the surgeon will gain access at a period early enough for extirpation of an intracranial neoplasm.

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REFLECTIONS ON SOME CRITICISMS OF THE PSYCHOANALYTIC METHOD OF TREATMENT.[1]

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Whatever else may be said about Freud's psychological theories and the psychoanalytic method of treatment none has denied the great significance of them in modern thought. It is becoming increasingly difficult for anyone interested in the problems of psychopathology, or, indeed, of psychology in general, to remain aloof from these theories, or to avoid ranging himself either in support of or in opposition to them. It would be out of place here even to attempt to indicate the significance they have for the sciences of sociology, mythology, and anthropology, as well as for psychology proper, but I wish at the outset to point out how necessarily fallacious it must be for anyone to reach any dogmatic conclusion as to their value so long as he confines himself to only one of their aspects. One of the best tests of the value of any new theory is to find out how fruitfully it can be applied, and the extent of the regions over which Freud's principles have been found to be valid—in regions relating to the activities of past ages as well as the present, to the psychology of the normal, of the neurotic, and the insane—is, perhaps, the most definite piece of confirmatory

[1] An address delivered before a joint meeting of the Chicago Neurological Society and the Chicago Medical Society, January 18, 1911.

evidence of the truth of them. In this paper, however, we are concerned with only one aspect of Freud's work, namely, the method of psychoanalysis that he has devised for the treatment of the psychoneuroses.

Those who hear or read for the first time of the psychoanalytic method may broadly be divided into two classes—namely, those whose interest is aroused though their intellect may be puzzled, and those who from the outset are repelled and adopt a hostile attitude. The line between the two classes is not a very sharp one, for I think it is true that no one has ultimately adopted the theory and practice of psychoanalysis without first having to overcome various difficulties and obstacles in his own mind. One might, therefore, more fairly say that readers show a great variation in the extent to which, in the further study of the subject, they are prepared to waive their own inevitable prejudices. To some the conclusions reached by Freud seem so grotesquely unlikely, and the objections to his method so obvious, that they do not feel it worth while to pursue the subject any farther. Others, equally conscious of the objections that immediately arise in their mind, are sufficiently openminded or tolerant to think it possible that perhaps their difficulties are due to their insufficient grasp of the matter, and that adequate explanations may exist which they will find if they pursue their inquiry. This latter position has this *a priori* consideration in its favor—namely, that many of the objections commonly raised are so extremely simple and obvious in character that it would be a highly remarkable occurrence if a man of Freud's recognized intellectual power had overlooked or ignored them. This consideration becomes the more probable when one recollects that assent has been given to the chief of Freud's conclusions by such men of scientific eminence and sane judgment as Professors Bleuler, August Hoch, Jung, Adolph Meyer, and Putnam. In view of this consideration it would seem unreasonable as well as unscientific to refuse to investigate Freud's conclusions, however strange some of them may at first sight appear. We have further to remember that most of us have a much more limited capacity than we flatter ourselves to have of assimilating new thought. As Nietzche well put it, "Mankind has a bad ear for new music." The history of new movements in culture and science is replete with instances that illustrate this sad fact, and yet how rarely does anyone draw the obvious lesson that they themselves will not find it easy to avoid the same danger when the opportunity is offered to them. There are names that live in history only because of the notoriety the bearers of them won by absurd denunciations of new thinkers, and one cannot help thinking that there are men at the present time who will be remembered by posterity for nothing else than their bitter hostility to the new teachings of psychoanalysis.

Of the principles of the psychoanalytic treatment itself I need

here say but little, for I have already on several occasions outlined them,[2] and I may assume that they are fairly familiar to you. Very briefly put they are as follows: It is a principle accepted by all psychopathologists, and no longer in discussion, that psychoneurotic symptoms are the product of underlying, dissociated mental processes, which are unknown to the patient, or, in Freud's sense, unconscious.[3] The symptoms are, therefore, substitutions of unconscious mental processes, and cease to exist when these are made fully conscious. Freud finds that the unconscious processes in question constitute an elaborate network of memories that centre around certain definite dynamic trends, or wishes, which are always of a sexual nature and are always connected with infantile experiences. They are incompatible, or out of harmony, with the rest of the patient's thoughts, and Freud holds that it is the conflict resulting from this fact that is the cause of their being split off, dissociated, or "repressed." They are under the ban of various inhibitions, or "resistances," and the patient automatically strives against acknowledging their very existence. Psychoanalysis is a method, having its special technique, that was devised for the purpose of overcoming these resistances, in order that the unconscious mental processes may be led back into consciousness. The chief aim of the treatment is to give the patient a better understanding of the innermost part of his mind, so that he may be in a position to divert the mental energy that was finding an outlet in the form of neurotic symptoms into more suitable and useful social channels. He cannot do this so long as the energy is locked up by unconscious fixations, so that it is necessary first to free it before it can be applied in healthier directions; it is a question of *reculer pour mieux sauter.*

The objections that have been brought against this method of treatment may for present purposes be divided into those concerning the practical using of the method and those concerning the theory of it. Most of them can be summarized in the statement that the theory is one-sided and largely untrue, while the application is harmful, impracticable, and unreliable.

It is easily demonstrable that some of the individual objections are, so to speak, not psychologically honest, in that they are only pretexts seized for the purpose of covering deeper ones, and often those who bring the objections are not conscious of the deeper roots of their antipathy to the method. It is, therefore, indispensable that we first say a few words about the relations of the subject to the normal. Freud maintains that the conflicts that lie at the base of neurotic conditions play an important and unavoidable part in the development of every one of us, and that on the out-

[2] Psychoanalysis in Psychotherapy, Jour. of Abnormal Psychol., iv, 140; The Psychoanalytic Method of Treatment, Jour. of Nerv. and Ment. Dis., May, 1910, p. 285.

[3] For an explanation of this term see Psychol. Bull., 1910, p. 111.

come of these conflicts depends whether a given person will be healthy or neurotic. In other words, the difference between a neurotic and a healthy person is not that the former has been subjected to conflict and the latter not, but that the two have reacted differently to similar conflicts. The whole matter is one essentially of childhood. We all know that an infant comes into the world destitute of the various social conventions and inhibitions that play such a large part in adult life. He is originally egoistic; cannot appreciate why his different privileges and impulses have to be regulated or interfered with; has at first no sense of the rights or feelings of others; will attempt to satisfy his bodily needs where and when he thinks fit; craves for food, attention, and other wants, quite regardless of external considerations. His early education consists almost entirely in learning to subordinate his personal desires and interests to considerations that at first only remotely appeal to him—in other words, it consists in constant adjusting of conflicts between internal and external situations. It is only gradually that such barriers are built up as modesty, shame, disgust, horror, moral feelings, and so on. Freud holds that the personal impulses, largely originating in various physical sensations, that are in this way renounced, are far more significant to the child than is generally supposed, and that the compromise thus demanded in its education is often arrived at only at considerable expense to mental health, and is often an imperfect one. A healthy person emerges from this series of conflicts by managing to replace the primary personal activities and interests by external social ones, and the mental energy of the former constitutes one of the main driving forces for the later acquired ones, being one of the chief bases for the whole later character of the person. The normal process, therefore, is repression plus satisfactory replacement, while what happens in the future neurotic is repression plus unsatisfactory replacement. Satisfactory replacement is termed sublimation, the energy, desires, and interests that were originally personal having been sublimated on to an impersonal, social sphere. In the neuroses, on the other hand, the symptoms are really a compromise between open expression of the original impulses and satisfactory replacement of them, or sublimation. In order to bring about normal sublimation, the impulses have first to be freed from their attachment to the neurotic symptoms.

The immediate bearing of these considerations is the conclusion that, as repression of certain primitive tendencies occurs in both the normal and the neurotic, one has to expect that both will show a resistance, which is merely the obverse of repression, against being made conscious of the repressed mental processes. This is, in fact, what is found. The normal person is shocked, and finds it incredible, when he is told of the great frequency with which in their childhood neurotic patients indulged in sexual phantasies in connection with

their parents. The reason is that the same thing is true of the normal, and he is resenting the information about the neurotic because really he is being told a disagreeable truth about himself. It is the people with secret attractions to various temptations who busy themselves most with removing those temptations from other people; really they are defending themselves under the pretext of defending others, because at heart they fear their own weakness. Similarly those who learn psychoanalysis regularly discover that the aspects of it that have most repelled them concern just the strongest and most deeply buried part of their own nature. In resisting these aspects they of course seize at all sorts of superficial reasons and excuses for thinking them untrue, but these are merely the cover for deeper personal grounds, the existence of which they are often unaware. In approaching the subject of the objections to psychoanalysis it is much more important to deal with this general truth than to argue about the superficial pretexts *seriatim*, and that is the reason why I have tried to emphasize it at the outset.

Taking up first the objections to the theory or principles of the treatment, we may first consider the most important—namely, to the effect that Freud attributes an exaggerated importance to sexual factors in the causation of the neuroses. Well, to begin with, there is a frequent misunderstanding in the minds of those who bring forward this criticism. They seem implicitly, if not explicitly, to take Freud's statements as if it meant that, according to him, the psychoneuroses are due to an unsatisfied desire for sexual intercourse, and naturally they triumphantly point to the obvious fact that a psychoneurosis may co-exist with full opportunities for gratification of this desire. Such critics evidently overlook the fact that the sexual instinct comprises a range of activities very much wider than this specific one. The commonest manifestation of the instinct—namely, love—frequently exists without any trace of desire for sexual intercourse, at all events consciously. Then all sorts of other activities, such as perversions, masturbation, and other autoerotic acts, obviously have to be called sexual, although their relation to sexual intercourse is very remote. There are many people, both men and women, who never have any desire for normal intercourse, but investigation shows that they have some other form of sexual life, often a very complex one. Psychoanalytic and other research has clearly shown that the desire for sexual intercourse is a highly specialized manifestation of the sexual instinct, and one relatively late in developing. It is preceded, and accompanied, by a great number of other sexual activities, some of which lead up to it, while others do not. It has been found that the instinct is a composite construction made up of several separate components. Distinct evidences of these components are to be observed even in early childhood, though the form they then take is very distant in appearance from what we call an adult sexual act.

It is impossible to go farther into this matter here, but those interested in it are recommended to read a translation that has just been published of Freud's *Drei Abhandlungen zur Sexualtheorie*.[4]

It has sometimes been asked why sexual disturbances should play such an essential part in the production of the neuroses as Freud maintains. Logically this question should be put after it has been determined whether they do or not, not, as is usually the case, before. It is entirely a question of facts. All I can say here is that no one who has conscientiously, and free from all prejudice, explored the dark regions of the mind where neurotic symptoms arise has any doubt about the essentially sexual nature of them. Freud says:[5] "Ich kann diesen Satz nur immer wieder von neuem wiederholen, weil ich es niemals anders finde, dass die Sexualität der Schlüssel zum Problem der Psychoneurosen wie der Neurosen überhaupt ist. Wer ihn verschmäht, wird niemals aufzuschliessen imstande sein. Ich warte noch auf die Untersuchungen, welche diesen Satz aufzuheben oder einzuschränken vermögen sollen. Was ich bis jetzt dagegen gehört habe, waren Aeusserungen persönlichen Missfallens oder Unglaubens, denen es genügt, das Wort Charcot's entgegenzuhalten, 'Ca n'empêche pas d'exister.'" These words were written six years ago, and others besides Freud are still waiting. Those who have learned the importance of the sexual factors in the neuroses have also come to realize that this fact is not so surprising as it at first appears, for they have learned that the stream that we call the sexual instinct is much broader and deeper than is commonly supposed. The very fact that the greater part of it flows in underground channels creates an extensive illusion as to its extent, but even consciously we cannot doubt that it plays the most important part of all the instincts. From it is evidently derived the main impetus that gives rise to artistic, literary, and poetic productions, and far more of our daily interests and ambitions than we superficially imagine are in reality sublimations from deeper and ultimately sexual sources. The various childhood conflicts above referred to concern almost entirely root manifestations of the same instinct, and anyone who has closely studied the steps by which infantile activities are transformed into non-sexual interests will be not at all surprised that frequently this delicate process does not proceed in the harmonious way that is necessary for the establishment of normal mental balance.

A critic might now remark: Granted all this, admitted that sexual factors are important, and perhaps the most important, agents in the causation of the neuroses; in view of the fact that most of them are unknown to the patient, why resuscitate them, what useful purpose can be served by delving into these disagreeable

[4] Three Contributions to the Sexual Theory, translated by Dr. A. A. Brill. Published in the Journal of Nervous and Mental Disease Monograph Series, 1910.

[5] Sammlung kleiner Schriften zur Neurosenlehre, 2e Folge, S. 103.

memories? This question involves two distinct matters, both of which, however, will be considered together—namely, the psychological explanation of the efficacy of the treatment, and the desirability or not of probing into a patient's innermost sexual life. The answer to the first of these questions was indicated above, when it was pointed out that the translation of the unconscious mental processes to consciousness necessarily signifies the harmonious fusion of mental elements that were previously in permanent conflict, and that the cessation of these conflicts carries with it the lasting cessation of the symptoms; the keynote here is that conscious knowledge of aberrant tendencies means a better and healthier control of them. As I have in a recent paper[6] fully discussed this matter, as well as the puerile allegation that the results of psychoanalytic treatment are due to suggestion, I will not deal with it further here. The second question is evidently based on the strong medical prejudice against handling sexual problems which is shown in so many ways, in the total exclusion of sexual subjects from the medical curriculum, in the marked disinclination to accept the sexual etiology of various diseases, and so on; the long fight, now settled, over the syphilitic origin of general paralysis was a striking instance of this. On the rare occasions when a sexual factor is mentioned in a medical text-book it is usually under the vague and misleading guise of "sexual excesses." This medical prudery is responsible for much harm, both to the profession who are thereby blinded to an important side of pathology and to the patients that consult them. Yet there is no reason to suppose that medical men outside their work are oblivious to the important part that sexual interests play in daily life. I remember on one occasion when I read a paper expounding the psychosexual origin of certain neuroses the opinion was freely expressed that sexual thoughts could not have such a hold on the minds of neurotic patients as I maintained they did. After the medical discussion an informal smoking concert was held, in which the main entertainment consisted in the relating of sexual and skatalogical anecdotes and recitations. I could not refrain from thinking of Heine's well-known stanza from the Die Heimkehr:

> Blamier mich nicht, mein schönes Kind,
> Und gruss mich nicht unter den Linden;
> Wenn wir nachher zu Hause sind,
> Wird sich schon alles finden.

This very nicely expresses the attitude in question. Only at home, in private, or in club life are such topics to be mentioned, not in scientific discussions, in public, "unter den Linden." Yet it is with this intimate, personal, and human side of neurotic patients that we are necessarily concerned, for it is in these deeper recesses of their nature that conflicts and disharmonies arise, not on indifferent and imper-

[6] The Action of Suggestion in Psychotherapy, Jour. of Abnormal Psychol., v, 217.

sonal topics. Evidently a given physician may from personal distaste refuse to investigate such matters, but he should recognize that by so doing he is allowing his personal prejudices to enter into a region where they do not belong—namely, scientific therapeutics. It is as though surgeons should officially proclaim that gynecological therapeutics is too distasteful for medical men to concern themselves with.

Critics who bring forward this objection usually cover their personal disinclination that lies at the root of it by contending that such a procedure is harmful for the patient. In this contention there is an undeniable modicum of truth. No one would maintain that exploration of a nervous patient's sexual thoughts and fancies contains no potentialities for harm, any more than that exploration of a parturient uterus by a village midwife contains no similar potentialities. But it must be remembered that while an investigation of sexual thoughts is not necessarily harmless, it is also not necessarily harmful. In other words, it is a therapeutic procedure that in this respect resembles most others—namely, its potentiality for harm depends almost entirely on how it is carried out. Are the operations of trephining or laparotomy fraught with no risk whatever, to say nothing of the preliminary administration of chloroform? The universal criterion of the advisability or justifiability of carrying out risky therapeutic measures is, or should be, the question of whether the probable good is greater than the possible harm. In such cases as those just instanced it is generally recognized that the potentiality for harm is much less in some hands than in others, and that by the adoption of suitable precautions this potentiality can often be minimized. Now it is contended for psychoanalysis that the various precautions that form part of its technique make it a definitely safe procedure. I should not like to assert that no harm can ever be done during psychoanalysis; it would, indeed, be strange if such a delicate procedure were safer than any other therapeutic procedure. Still, I will say that, in spite of vague statements to the contrary, no case has come to my knowledge where harm has been done to the patient through this treatment, and no one who is familiar with the facts will deny that at all events far more good than harm is done. It is perhaps not out of place here to say a word of warning concerning those physicians who blindly rush into a psychosexual investigation under the name of psychoanalysis, but without any proper training in the matter. It should be obvious that psychoanalysis, perhaps more than any other therapeutic measure, needs a careful, disciplined study before it can be adequately applied or judged.

Another very prominent objection brought against the psychoanalytic treatment is that it is said to be unreliable. This applies partly to the main theory, but especially to the interpretations of the patient's symptoms, utterances, and other mental material. Into the construction of the theory, as into that of all theories, it

is plain that various preliminary hypotheses have entered; but it is maintained that these are the reverse of fanciful, and are always direct and legitimate inferences from facts objectively gathered. Freud himself says:[7] "Ich setze keinen Stolz darein, die Spekulation vermieden zu haben; das Material für diese Hypothesen ist aber durch die ausgedehnste und mühevollste Beobachtung gewonnen worden." The question of actually proving in detail the various parts of the theory is technically an extremely difficult one, both for psychological reasons connected with the meaning of what constitutes scientific proof, and for extrinsic reasons, some of which will presently be mentioned. It has been said that up to the present not sufficient material has been published to establish either the truth of the theory or the value of the treatment. I sometimes think that those who make this statement are unaware of the extent of the material that has been published by the Freudian school. There exist some twenty-five books on psychoanalysis, five periodicals are entirely devoted to the subject, while the number of papers runs into many hundreds. Nevertheless, I freely admit that, in spite of this, not enough observations have yet been published to prove scientifically every inference and interpretation that has been made. On the other hand, we contend that enough has been published to demonstrate the principles of the method, to show the truth of a number of detailed inferences based on the application of it, and thus to establish the right to ask that the other inferences be not denied by critics who have not personally investigated them. A word must also be said about the actual difficulties of publishing cases, which are much greater even than they appear. It is not merely that absolute general precautions must be taken to conceal the identity of the patient, but minor points in the analysis that show the validity of it have to be suppressed, for it is just those that would betray this identity. Then, again, a given interpretation, which can be put in a sentence, may be based on several hours of detailed observation, most of which, the individual utterances of the patient, the tone, the emotional gestures, etc., are impossible to reproduce, although it is just these that inevitably convince one of the validity of the inference drawn.

There are, however, much deeper reasons why many of the individual psychoanalytic interpretations seem very unlikely and often strained. It is evident that the connections between different thoughts proceed, or are supposed to, along paths quite foreign to our normal, more or less logical, thinking processes, and that is why anyone who reads of them repudiates them as highly improbable. It is often forgotten, however, that they cannot fairly be compared with logical thinking, for they represent the workings of unconscious mental processes which are demonstrably quite different from our conscious ones. If, for instance, the conscious atten-

[7] Sammlung, op. cit., S. 100.

tion is designedly distracted during a word-association experiment,[8] it will be found that the intrinsic or logical reactions are largely replaced by superficial ones, especially by sound connections; in other words, the more automatic and less conscious mental functioning becomes the more does it proceed by means of superficial connections of the kind familiar to psychoanalysts. I cannot now go farther into the psychological questions here involved, but I wish to draw special attention to the following important consideration. There is every reason to believe that in the normal as well as in the neurotic there exists a strong general resistance to what may be called symbolic thinking, that is, to mental processes that proceed by means of analogy, superficial connections, and so on; in fact, our logical tendencies rightly repudiate what seems to us to be an absurd, irrational mental procedure. Yet in children and savages, during intoxication and insanity, in superstitions, folklore, and even in poetry, there is no doubt that metaphor, analogy, and symbolism play a very large part, sometimes even as large as they do in unconscious mental processes. A little study of the sources of dream material is enough to convince anyone of how extraordinary are the superficial connections that are formed in their mind quite unknown to them. It is often further asked what guarantee one has in psychoanalysis that a given interpretation is correct. It would take too much time fully to answer this, and I can only assert that in the psychoanalytic technique special provision is made for objective criteria and tests of the truth of any given interpretation; the whole method is the very reverse of the vague, uncontrolled, and speculative procedure it is sometimes represented to be.

Very little need be said concerning the objections to the practicability of the psychoanalytic method of treatment, for to anyone who has assimilated the preceding considerations these objections will answer themselves. It has been said that the method is of extremely limited applicability on account of the time and, therefore, expense involved, of the number of cases that are intrinsically unsuited for the treatment, of the difficulty of using it with hospital patients, and so on. It is quite easy to see that the motive of these objections is to depreciate the treatment, rather than to criticise it seriously, for if the enormous value of it were generally recognized one cannot doubt that these difficulties would lose much of their weight, and would be to a great extent overcome. They can most shortly be met by comparing for a moment psychoanalysis with the sanatorium treatment for tuberculosis, for when this was first instituted exactly the same objections were raised: it was a mode of treatment applicable only to the rich; it involved a great expense of time and money and the training of a special class of physicians; was suitable for only certain selected cases; had considerable

[8] See Jung Diagnostische Assoziationsstudien, 1906, Band i, S. 104, etc.

potentialities for harm, and so on. But when it became realized that the open-air treatment gave the most effective results; that the long duration of it was something inherent in the circumstances; that there was no adequate alternative to it; that, in fact, to ignore it was tantamount to not doing the best for those afflicted with tuberculosis, then the difficulties were rapidly overcome, even for the poorest hospital patients. No doubt it is more satisfactory when we can achieve rapid cures of constitutional maladies, a fact that partly explains the gratification with which the recent Ehrlich-Hata discovery has been received. Still, it must be remembered that from the very nature of things there are certain modes of treatment which it is dangerous to press forward too rapidly, such as the reëducation of the system by means of tuberculin, antirabic and other vaccines. Psychoanalysis, which is essentially a reëducative treatment that modifies mental trends of many years' standing, is just such a treatment where it is impossible to press. As a matter of fact, it compares very favorably in many respects with the sanatorium treatment of tuberculosis, for it requires less time, no special apparatus, buildings, nursing staff, and so on, and, above all, can be carried out in an ambulatory service when the patient is about his ordinary work; indeed, it is very desirable that the patient should have some employment or other interest unless he is totally incapacitated. As to the limited scope of the treatment, we already find in practice that there is a wide range over which it is conveniently applied, and there is no doubt that with the goodwill of the medical profession this range would be very considerably extended; although many intrinsic difficulties exist, many of the alleged ones are largely fictitious, being invented or exaggerated by those who really oppose the treatment on other grounds.

In these few remarks I am fully aware that I have not enumerated all the objections that have been brought forward against the psychoanalytic treatment, and have not even fully discussed any one of those I have mentioned, but I trust I have succeeded in my aim of illustrating the fact that there do exist answers to all of them which in the opinion of those who have properly investigated the matter are entirely adequate.

APLASTIC ANEMIA, WITH REPORT OF A CASE.

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The red corpuscles of the blood are subject to constant loss and replacement. The best evidence of their continuous destruction

within the body is the continuous flow of bile pigment, a derivative of hemoglobin. Red cells are also lost by hemorrhage, internal and external, slight and severe. In the female, menstruation periodically removes large numbers. In health, of course, an equally constant formation of new corpuscles in the red marrow maintains the number at the normal level.

It is obvious that a deficiency of red cells, that is, a condition of anemia, might result from excess in the destructive processes or from deficiency in the reconstructive functions. There is still much obscurity as to the relative importance of these two factors in the different anemias, but it is probable that in the majority the chief causative factor is increased destruction. As a result of this primary loss of hemoglobin-bearing cells, and by way of compensation for it, changes take place in the marrow, and new corpuscles are poured into the blood in increased numbers. If the loss of red cells is extreme, the stimulation of the erythropoietic functions may be so great that the spleen and other organs not normally concerned in the production of red corpuscles may assume this role, or, more properly, resume it, since it is one of their normal functions in the embryo. Thus, the degree of anemia depends not only upon the severity of the process which is destroying the red cells, but also upon the efficiency of the compensatory regenerative processes. Schaumann[1] compares this mechanism to the way in which the functional efficiency of a diseased heart depends not only upon the severity of the valvular leak, but also upon the degree of compensatory muscular hypertrophy. This paper is a study of certain anemic conditions, in which the compensatory processes are strikingly deficient. In classifying the anemias on the basis of blood examinations, three types stand out with fair distinctness. In their clinical and anatomical features the cases correspond fairly well with the same grouping.

1. The orthoplastic or benign group includes nearly all the anemias secondary to definite morbid states—infections, neoplasms, parasites, chronic intoxications, as well as chlorosis, anemias from acute or chronic hemorrhage, or from faulty hygiene and nutrition. The hemoglobin is reduced in greater proportion than the reds (low color index). Qualitative changes, as seen in smears, are, except for achromia, usually slight in proportion to the severity of the anemia. The average size of the reds is normal or smaller than normal (low volume index), and if nucleated reds are present, they are mostly normoblasts. The anemia itself is often of little clinical importance. Even though severe, it remains essentially benign, and recovery is to be expected with removal of the cause. The yellow or fatty marrow of the adult is changed partially or completely to red, cellular marrow, but it is always normal red marrow, with great preponderance of normoblasts and neutrophilic myelocytes. The change is quantitative rather than qualitative. Obviously such marrow is capable of producing more blood cells

than before. It has undergone compensatory hyperplasia, in order to make up the loss of cells incident to the causative disease.

2. The metaplastic or pernicious blood picture is seen chiefly in the condition or conditions known as pernicious anemia. The anemia produced by infections with Bothriocephalus latus is also of this type, as a rule, and, exceptionally, syphilis, hepatic cirrhosis, and other diseases commonly producing anemia of the benign type will cause instead a metaplastic change. The blood picture is characterized by high color and volume indices, the increased size of the red cells being perhaps the most important feature. The reds show marked changes in form and color. Megaloblasts are almost always found, and they exceed the normoblasts in number. Clinically, the anemia is a much more serious matter than in the first group. Its course is malignant and usually fatal. At autopsy the normal yellow marrow is found to be universally replaced by red celluluar tissue. The changes are not only more intense than in the benign forms, but they are different in quality, the principal histological peculiarity being the increase in megaloblasts.

The known facts concerning those conditions in which the pernicious picture occurs as an obviously secondary manifestation, particularly in Bothriocephalus infections — conditions which frequently recover when the cause is removed — these facts seem to indicate that the changes in the blood and marrow represent a reaction of the hemopoietic organs to long-continued, perhaps specific, destruction of corpuscles. We do not know whether compensation is more efficient or less efficient than in the orthoplastic cases, so far as the capacity for turning out new cells is concerned. Nor can we say, at least in regard to some, that the marrow has not been injured beyond repair. But it is safe to assume that the destruction of red cells has been extreme, and the reaction on the part of the blood-making organs very intense.

3. The aplastic type of anemia is very rare, but its great theoretical significance makes it worthy of the closest study, for much light will be shed upon the nature of the processes by which the erythropoietic organs repair an anemia by a consideration of the exceptional cases in which those reparative processes fail to occur. Clinically the cases show considerable variation. They are alike, however, in the rapid advance of the anemia and the promptly fatal termination. The case presently to be described is, I believe, the only one in which a remission has occurred after the aplastic features have been clearly recognized. Hemorrhages are present in most cases, varying in severity from a few scattered petechiæ to severe hemorrhagic purpura. Other than this the cases show clinically only the features common to all grave, rapidly advancing anemias.

The blood picture is striking and easily recognized. The anemia advances so rapidly that the reds and hemoglobin are usually very low at the first observation. The color index is usually low. The red corpuscles as seen in smears show but slight changes in form

and coloring, even though their numerical reduction is extreme. Nucleated reds are absent or present only in very small numbers. Remarkable changes occur in the leukocytes, the total number being greatly decreased, this decrease involving only the granular forms. The lymphocytes remain present in their normal numbers, while the polymorphonuclear neutrophiles, eosinophiles, and mast cells are absolutely and relatively diminished. This loss of granulocytes is extreme. Mast cells and eosinophiles are often entirely lacking, and sometimes even the neutrophiles can be found only by searching. Platelets are also greatly decreased. The essential features then so far as the blood is concerned are intense loss of red cells and granular leukocytes—those blood elements, and only those, which have their origin in the bone marrow. It is to the marrow then that one looks for an explanation of the disease.

The macroscopic changes in the marrow are not uniform. Sometimes this tissue is yellow or gelatinous, sometimes red and cellular, sometimes mottled, while in rare instances it is replaced by connective tissue (Assmann[12]). The microscopic findings vary correspondingly, but they are alike in the absence of the cells from which the missing blood elements are derived. In the most typical cases the marrow is yellow, and consists of fat. Erythroblasts, myelocytes, and other cells having to do with the formation of blood corpuscles are few in number or completely lacking. Sometimes smears show only debris without cells. Either the marrow is so extensively diseased that it cannot perform its functions, or it fails, for some unknown reason, to do so in spite of the usual stimulus. This inability of the marrow to respond explains why the cases progress so rapidly and why the characteristic blood picture develops.

In certain cases, though they may not be distinguishable, clinically or hematologically, from those already described, the marrow is red and cellular. Microscopically, however, it is neither normal red marrow nor the megaloblastic tissue of pernicious anemia, for both nucleated red cells and myelocytes are lacking or nearly so. In their place there are found only lymphocytes.

Concerning the significance of this change, there has been considerable controversy. Some consider that the presence of the lymphoid tissue is secondary to the disappearance of the normal marrow structures. Others hold that the lymphoid hyperplasia is primary and that the overgrowth of this foreign tissue has led to the disappearance of the normal marrow elements. It is probable that both views are partially correct, some cases being of the one sort, some of the other.

That primary hyperplasia of lymphoid cells may cause aplasia of the red elements is shown by a case reported by Türk.[2] A typical myeloid leukemia changed to what appeared to be lymphatic leukemia. Shortly before death there was a rapid increase of the anemia, with a decrease of white cells to 940 per c.mm., of which

but 6 per cent. were neutrophiles—a typical aplastic picture, involving both the red and white elements. At autopsy the marrow showed lymphoid hyperplasia with almost complete absence of other normal cells. Here there can be little doubt that the aplasia was the result of the crowding out of the blood-forming cells by the overgrowth of the lymphoid tissue.

On the other hand, there are cases, like that of Hirschfeldt,[3] in which it seems equally certain that the lymphoid change in the marrow was secondary to exhaustion of the normal erythroblastic tissue. Here a woman died after an illness of nine months which followed parturition, resembled pernicious anemia, and was marked by profuse hemorrhages. Again, Blumer's case[13] was typical aplastic anemia, associated with lymphoid hyperplasia of the bone marrow. The latter was partly fatty and partly red, from areas of intense lymphoid hyperplasia. The author points out that, as the lymphoid tissue did not occupy the whole marrow cavity, the aplasia could not be explained by mechanical crowding out of the normal elements by the new tissue.

Most cases of aplastic anemia with lymphoid marrow must, however, remain puzzles for the present. Such cases are those of Wolff[4], Senator,[5] and Michaelis.[6] Senator considers them leukemias or pseudoleukemias. Blumenthal and Morawitz,[7] on the other hand, believe the disappearance of the normal elements to be the primary change. Morawitz and Rehn[8] consider the predominant cells in these cases to be not lymphocytes, cells foreign to the marrow, or at least not specific marrow elements, but very early stages of the normal granular leukocytes, that is, promyelocytes or myeloblasts.

A case seen in consultation with Dr. H. H. Germain perhaps belongs to this class. It appeared at first to be noma, and the patient did well for a week after operation. Then he became much worse, and an examination of the blood showed 70 per cent. of hemoglobin, 2,472,000 red corpuscles, and 5000 leukocytes. Nucleated reds were rare, and abnormalities in shape and coloring were but slight. One and only one neutrophilic leukocyte was found during a long search. There were no eosinophiles or mast cells; practically all the white cells were lymphocytes. Perhaps this was lymphatic leukemia with secondary infection of the mouth, perhaps primary infection of the mouth, sepsis, and exhaustion of the marrow, especially in its leukoblastic functions, with disappearance of the granulocytes and secondary or vicarious lymphocytosis.

Such cases are hard to explain. Some of them ought not to be classed as aplastic anemia at all, since the aplasia involved the leukogenic rather than the erythrogenic structures. These two functions are often more or less dissociated in diseases of the class under discussion, sometimes markedly so, as in a case reported by Türk,[9] where, in a case of penumonia and septic endocarditis, the granular leukocytes all but disappeared, the reds remaining normal.

But the anatomical relationship of the cells having to do with the two functions is so close that one can hardly be much affected without involving the other.

There is ample experimental evidence that lymphoid marrow may occur entirely apart from leukemia or related diseases, that it may result from causes commonly leading to anemia, and that the associated blood picture may give evidence of inadequate regenerative activity on the part of the marrow. For the details, the reader is referred to the papers of Blumenthal and Morawitz,[7] Hirschfeldt,[10] Morawitz and Rehn,[8] and Morris.[11] The anemia was produced in these cases by bleeding or by the injection of toxic substances. The results must be applied to the explanation of human aplastic anemia only with great caution, as the blood pictures in the experimental animals differed in important respects, such as the persistence of a normal proportion of polymorphonuclear neutrophiles, from that of the disease in man. But they at least prove that lymphoid marrow does not always signify leukemia.

In some cases it is probable that the lymphoid change is more apparent than real, the lymphocytes not being themselves markedly increased or decreased, but being merely what is left after other cells, normally predominating, have been removed. It is probable that the condition of the marrow previous to the onset of the aplasia has an influence on the histological conditions found at autopsy. One would hardly expect to find the same thing in a previously healthy adult in whom a severe hemorrhage has failed to call forth the usual regenerative changes in the fatty marrow, as in a child, or in a person in whom aplasia is but a terminal event in an illness of a sort usually associated with red marrow. In fact, several writers refer to the lymphoid tissue in their cases as being loosely packed, and suggesting normal marrow minus everything but lymphocytes, rather than the intense infiltration of leukemia.

Concerning the pathogenesis of aplastic anemia, it is conceivable that such a condition might arise from incapacity of the blood-forming organs alone, but in most cases at least there is doubtless also the factor of increased destruction of red cells. Thus, Aubertin[14] distinguishes "anémie *par* anhématopoiése" and "anémie *avec* anhématopoiése." Anemia *from* anhematopoiesis is seen only in leukemia or other destructive disease of the marrow. Simple primary aplasia of the marrow does not exist, and, except in these conditions, aplastic anemia is always anemia *with* anhematopoiesis, one of the usual causes of anemia always being present. This view is also held by Pappenheim.[15] Hemorrhage, sepsis, the unknown noxus of pernicious anemia, or some other agency causes an acute anemia, and the usual compensatory regenerative changes in the marrow fail to occur, perhaps because the same agency that caused the anemia has also injured the marrow. Aplastic anemia is not, therefore, a disease of itself, but merely a condition which may arise in anemias from various causes.

In discussing the etiology of aplastic anemia then we must consider what forms of anemia are likely to have this unfortunate complication. Hirschfeldt[3] describes a case in which typical pernicious anemia changed, after severe hemorrhages, to aplastic anemia. Lavenson[16] discusses at length the relations between aplastic and pernicious anemia, and concludes that the former is always a variety of the latter, the differences resulting entirely from the absence of regenerative processes in the aplastic cases. I doubt, however, whether we are justified in making such a sweeping statement. Existing knowledge of the nature of pernicious anemia is limited. We recognize the disease only by observing its clinical course and its hematological features. In the presence of aplasia, this course is greatly modified, and the blood picture, depending as it does on the peculiarities of the regenerative processes in the marrow, are wholly different where these processes fail. Such cases as that of Hirschfeldt, just quoted, are very rare. Aplasia very rarely occurs in preëxisting pernicious anemia, and the compensatory processes in the marrow usually persist to the end. The patient with ordinary pernicious anemia dies, not because regeneration of the destroyed blood elements fails, but because compensation, intense as it is, is no longer able to keep pace with the still more intense hemocytolysis. If aplastic anemia is merely pernicious anemia without compensatory regeneration, that failure of regeneration exists from the first in the vast majority of cases, and, I repeat, our knowledge of pernicious anemia is still far too meagre to permit us to affirm or deny its presence in the absence of all its common diagnostic features.

There is, in fact, excellent evidence that aplasia of the erythroblastic tissues may complicate anemias which are not of the pernicious type. Ehrlich's classical case,[17] which Lavenson includes in his list, followed acutely after uterine hemorrhage the result of abortion in a previously healthy young woman. Hirschfeldt[18] mentions a case in which the disease followed acutely after a severe hemorrhage.

The following case, which occurred on the service of Dr. E. B. Young at the Boston City Hospital, is of similar origin: A perfectly healthy girl, aged sixteen years, suddenly began to flow profusely. After two weeks she was brought to the hospital and much blood clot was evacuated from the vagina. A condition resembling purpura hæmorrhagica rapidly developed, with hemorrhages from gums and skin. The heart was slightly enlarged, with systolic and diastolic murmurs, and a pericardial friction rub. The hemoglobin was 35 per cent., the red corpuscles 1,338,000, and the leukocytes 6000. There were 12 per cent. of polymorphonuclear neutrophiles, 86 per cent. of lymphocytes, 1 per cent. of large mononuclears, and 1 per cent. of stimulation cells. Platelets were almost absent from the smears. Nucleated reds were rare, and no other abnormalities

in these corpuscles were noted. She died in a few days. Autopsy was refused.

Cases are reported by De Massary and Weil,[19] Steinhaus and Stordeur,[20] Muir,[21] and Blumenthal,[22] in which hemorrhages played an important part, but the circumstances were such as to make it doubtful whether they were the cause or the effect of the blood disease. But when hemorrhage appears suddenly in a previously healthy individual, as a result of such a well-known and adequate cause as abortion, and where aplastic anemia follows directly and acutely, it seems unnecessary to drag in a hypothetical, preëxisting, pernicious anemia.

Quite recently, Selling[28] has reported several cases of anemia of the aplastic type due to benzol poisoning, and refers to experiments, not yet published in detail, in which the condition was produced in animals by the same agent. Furthermore, true secondary anemia may be complicated by aplasia. Thus, Hertz[29] describes 2 cases in which sepsis seemed to be the important etiological factor. Kranz[23] reports a case of aplasia in anemia from Bothriocephalus latus. Schur and Löwy[24] describe a case after corrosive poisoning. Schwartz's case[25] followed renal abscess in a child, the aplasia involving principally the leukoblasts. One of Blumenthal's[22] had syphilis. Berberis' case[26] followed miscarriage, with hemorrhage and sepsis. Finally, Dickson,[27] in his monograph on the bone marrow, describes and figures degenerative conditions in the marrow of several long-standing cases of sepsis, tuberculosis, and cancer, which he attributes to increased activity followed by exhaustion of the blood-forming cells. Unfortunately, no blood reports are given.

In conclusion then it seems altogether probable that aplasia of the marrow may occur in post-hemorrhagic or destructive anemias of any sort, possibly as a result of direct action of the same toxins which destroy the blood cells, possibly from exhaustion by overactivity.

The prognosis in aplastic anemia is unfavorable. With the possible exception of acute leukemia, no disease of the blood is so rapidly and uniformly fatal. So far as I am aware, the case to be reported is the only one in which even temporary improvement has occurred.

Treatment has not been effectual. It does not seem likely that any drug will have the least influence. Direct transfusion should certainly be done when the condition complicates hemorrhage, and, perhaps, in other cases following acutely after definite causes.

For the privilege of reporting the following case, as well as for material assistance in studying it, I am indebted to Dr. C. B. Wormelle, of Brighton, Massachusetts:

Sherman S., aged five years, had been ill six weeks when I first saw him in consultation with Dr. Wormelle, on June 15, 1907. There was nothing in his past history of importance, except an attack of measles, with pneumonia, several years before. At the beginning of his illness, he was sleeping in the same room with his

brother, who was at the time suffering from chronic suppurative disease of the bones, with discharging sinuses on the face and in the groin. This child has since recovered. Sherman's symptoms were those of a rapidly advancing anemia, with irregular fever, often as high as 103°. His only complaints were weakness and slight abdominal pain. Examination showed a well-developed but poorly nourished boy. He was apparently very ill, stupid, and irritable, resisting examination. He was very pale, with the yellow tinge so suggestive of pernicious anemia. There was a small hemorrhagic spot on the forehead, which his mother could not explain. The heart was slightly enlarged to the left, and presented systolic and diastolic murmurs. The other viscera were normal. There was no enlargement of the liver, spleen, or lymph nodes. There was no edema. The reflexes were normal. There was a slight Kernig sign, but no rigidity of the neck. The eardrums were normal.

On the basis of the blood examination, a diagnosis of aplastic anemia was made, and an unfavorable prognosis given. The unexpected happened, however, and he promptly recovered. His color became good, the heart murmurs disappeared, and at the end of a month he was apparently as well as ever.

In October of the same year a large ecchymosis suddenly appeared in the right groin, and the old symptoms recurred, with rapidly advancing anemia and high fever. When seen by the writer, on November 11, his condition was about the same as in June. The spleen was still normal, but the liver edge was palpable, and lymph nodes, varying from a quarter to a half inch in diameter, could be felt in the groins, axillæ, and neck. A slight nose-bleed had just occurred. Minute punctures made for the purpose of obtaining blood either bled profusely or caused tender, hemorrhagic swellings. On November 16, about a month from the beginning of the relapse, the child vomited a large amount of blood, and died.

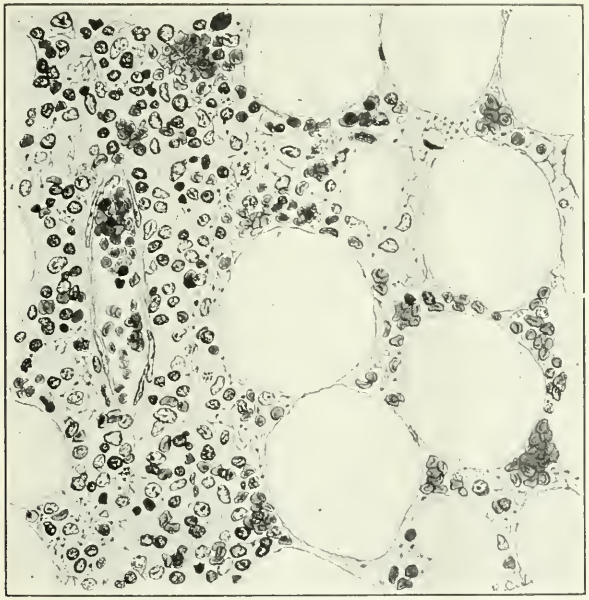
	June 10.	June 15.	July.	November 11.
Hemoglobin, per cent.	40% (Tallqvist).	12% (Sahli).	85% (Tallqvist).	25% (Sahli).
Red corpuscles.	2,000,000	790,000	3,700.000	1,500,000
White corpuscles	6000	1970	Decreased	5030
Polynuclear neutrophiles	....	8.8 per cent.	....	3.2 per cent.
Lymphocytes	....	88.0 "	....	90.8 "
Large mononuclears and transitionals	....	1.2 "	....	0.4 "
Eosinophiles	....	0.0 "	....	0.0 "
Mast cells	....	0.0 "	....	0.0 "
Myelocytes (neutrophiles)	....	0.4 "	....	0.4 "
Stimulation cells	....	1.6 "	....	5.2 "
Erythroblasts per c.mm.	....	21	....	
Megaloblasts seen	0	2	0	0
Normoblasts seen	0	1	0	1
Changes in reds	....	Slight	....	Slight
Size of reds	....	Small	....	Vol. index 0.69
Platelets	....	Much decreased	....	Almost absent

The blood findings are shown in the table. The first two columns show the rapid advance of the anemia, the reds falling from 2,000,000 to 790,000 in five days. In spite of this low figure, the reds appeared almost normal in smears, and nucleated forms were present only in small numbers. The decrease of platelets was obvious. Leukopenia was striking, and involved the granular leukocytes to a marked extent, the actual number of polymorphonuclear neutrophiles per cubic millimeter being but 173 instead of the normal 4000 to 6000. Eosinophiles and mast cells, likewise formed in the marrow, were absent. The third column shows the extent to which the blood recovered in the remission. The final column shows the blood in the relapse, a week before death. The anemia had not yet become remarkably severe. The volume index, which expresses the average size of the red corpuscle referred to 1 as normal, was estimated after the method of Capps,[30] except that the corpuscles were sedimented spontaneously instead of by the centrifuge.[32] The low figure is like that of benign anemia, and in contrast to the high values commonly seen in pernicious anemia. The leukocytes are higher than before, but there is the same decrease of the granular forms, the absolute number of neutrophiles being 161 per c.mm. The lymphocytes (4577 per c.mm.) are not beyond the normal limits for a child aged five years. On the whole, these are typical pictures of aplastic anemia.

An autopsy was performed by Dr. Timothy Leary, who, it is much to be hoped, will later report upon it at length. There were no important abnormalities except those having to do with the blood and blood-forming organs. The esophagus contained a large clot, and there were small petechial spots on the mucous and serous surfaces. The marrow of the vertebræ was pale red. That of the femur was yellow and jelly-like, and mottled with red. The microscope showed typical fat tissue with abundant hemorrhage between the fat cells, apparently the cause of the red mottling seen in the gross specimens. Here and there about the arterioles there were small islands of nucleated cells. These were almost exclusively lymphocytes. Nucleated red corpuscles, normally so abundant, were very rare, and were small in size. A single group of megaloblasts was found after long search. Granular leukocytes were also rare. Neutrophilic myelocytes, so abundant in normal red marrow, were only found after careful searching. But one eosinophile was seen. There was a diffuse infiltration of the lymph nodes and of the interlobular connective tissue of the liver, with lymphoid cells somewhat suggestive of lymphatic leukemia. The spleen, otherwise normal, contained immense numbers of large epithelioid cells, within which were masses of yellowish-brown pigment.

The red color of the marrow was not due to the presence of regenerative cellular changes, but to hemorrhages, which were present in many other parts of the body as well. The marrow was essen-

tially aplastic, the aplasia involving the leukoblastic (granulocytic) as well as the erythroblastic elements. There is, to be sure, a *relative* increase of lymphocytes in the marrow as well as in the other tissues, somewhat suggestive of lymphatic leukemia, but it must be remembered that the patient was a child, aged five years. At this age the lymphatic apparatus is very active and readily responds to stimuli, and the number of cells of this type is, both in the blood and in the tissues, greater than in the adult. No diagnostic significance then can be given to this finding, nor to the slight increase of lymphocytes in the last examination of the blood. The case is surely not one of replacement aplasia. The amount of lymphoid tissue is at no point great enough to have



Bone marrow of Sherman S. Aplastic anemia. Cell island about a small artery on left of picture. Cells mostly lymphocytes. Hemorrhage into tissues between fat cells.

influenced by its presence other normal structures. The microscopic picture is red marrow minus everything except lymphocytes. Disregarding the hemorrhages, the prominent feature is replacement of normal cells by fat. The lymphocytes have not been thus replaced, but they are themselves little if at all increased.

The rarity of giant cells and the concomitant rarity of platelets is in complete accord with the views of J. H. Wright as to the origin of these bodies.[31]

It is difficult, perhaps at present impossible, to determine the primary cause of the anemia in this case. The yellow color of the skin, the marked remission, the iron-containing pigment in the

spleen, and the single group of megaloblasts found in the marrow suggest pernicious anemia, but, considering the uncertainties and qualifications imposed by our present lack of knowledge of the disease or diseases known by that name, it is perhaps safer not to venture a diagnosis. Some unknown agency caused this child to become anemic, probably through destruction of red corpuscles. For a time the marrow failed to react, perhaps because it suffered injury from the same noxus. The remission was probably due to temporary recovery on the part of the marrow, since it seems unlikely that this tissue in the condition found at autopsy could have replaced the lost cells so promptly, even if the hemolytic agent ceased its activity. Finally, aplasia again supervened, with or without exacerbation of the destructive process, and from this second attack the child died.

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GRANULOMA PYOGENICUM (BOTRYOMYCOSIS HOMINIS OF THE FRENCH).

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In 1897 Poncet and Dor[1] first described a neoplastic, fungating, pedunculated growth occurring in man, in some respects similar to the so-called botryomycotic tumors at times seen in domestic animals. The growths were pea- to nut-sized, reddish in color, and developed by means of a pedicle from the derma. Histologically, their structure was that of a typical granuloma.

Poncet and Dor found numerous yellowish, mulberry-shaped masses of cocci, which they believed to be identical with the botryomycosis (Bollinger). Their findings were partially confirmed by Nocard and by Leclainche, but later investigators, including Bodin,[2] Crocker,[3] and Hartzell,[4] have shown that these bacterial collections consist entirely of ordinary yellow staphylococci. Why the presence of these organisms should occasionally give rise to this particular type of abnormal cell proliferation is not known (the fibro-adenoma theory of Carriere and Potel, which was founded on the accidental occurrence of a coil gland in one of the tumors, is unquestionably erroneous, and has been generally rejected), but the phenomenon is probably similar in many respects to that observed in the highly vascularized tissue which is commonly known as "proud flesh." Owing to the location of the microörganisms, it is practically impossible to bring about a cure by means of the topical use of antiseptics alone, and a lesion may persist for months in spite of treatment. The pedicle is composed of connective tissue, with numerous bloodvessels, and profuse hemorrhage results when it is severed. Even when the growth is removed in this manner it promptly recurs unless the base is thoroughly cauterized.

The condition is not an extremely infrequent one, and the following typical instance is reported, not because of its rarity, but more for the purpose of calling attention to the clinical features of the lesion, in order that it may be more readily recognized when encountered.

H. M., aged nine years, female, schoolgirl. Referred to me by Dr. J. M. Allen, of Liberty, Mo.

Family History. The cutaneous history of the family is negative.

[1] Trans. Congrès de Chirurg. de Paris, October, 1897.

[2] Ann. de dermat. et de syph., iii, 289.

[3] Diseases of the Skin, 3d edition, ii, 1081.

[4] Jour. Cutan. Dis., xxii, 520.

Personal History. The patient is a native of Missouri, and a resident of Missouri City, Mo. She has never had a serious illness, and has never before suffered from a skin disease.

Present Illness. Seven weeks prior to the time of consulting me a small furuncle developed on the back of the patient's left wrist. A few days later this was opened and drained by Dr. Allen, and an antiseptic dressing applied. The parents were instructed to renew the gauze compresses twice daily, carefully cleansing the part with an antiseptic solution every time the dressing was removed. One week later the patient returned to Dr. Allen for further advice.

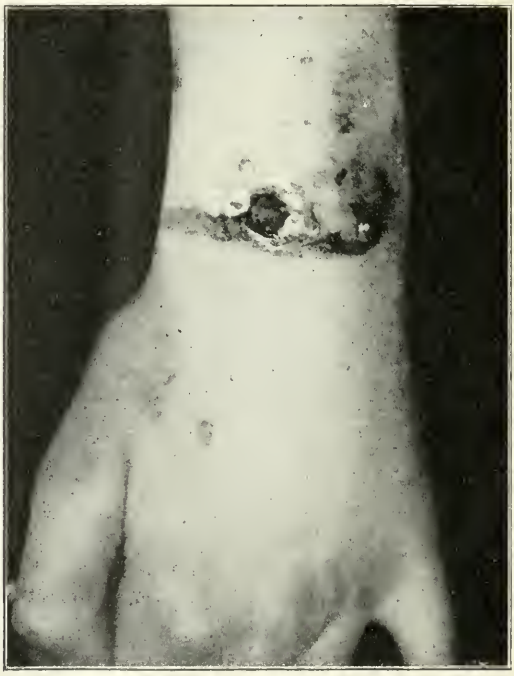

Fig. 1.—Lesion on back of wrist.

On examination it was found that a small, bright red, pedunculated tumor, the size of an ordinary pea, had sprung up through the opening left by the furuncle. The skin surrounding the lesion was reddened and tender, and there was considerable suppuration. The tumor itself was plum-shaped, with a smooth, moist surface, and was attached to the derma by means of a slender pedicle about 0.5 cm. in length. The growth gave rise to no pain, but was tender to the touch. A stronger antiseptic was prescribed, to be used in conjunction with an astringent dusting powder. In spite of careful and conscientious treatment, however, the tumor continued to

increase in size, and a suspicion was aroused that it might be malignant in nature.

The patient was a blonde, with a fair, smooth, soft skin. A careful general examination revealed nothing abnormal, except a slight enlargement, with tenderness, of the epitrochlear and axillary glands on the left side. On the dorsal surface of the left wrist was an irregularly outlined area of reddened, inflamed skin, measuring 4 by 5 cm. Near the centre of this patch was a small, mushroom-like tumor, cherry-red in color, and soft and compressible to the touch. The pedicle was attached below to the derma, and was not adherent to the broken epidermal wall which surrounded it above. Cultures made from the pus, by Dr. Frank J. Hall, of this city, showed a pure growth of Staphylococcus pyogenes aureus.

Fig. 2.—Nodule, actual size.

A diagnosis of granuloma pyogenicum was made, and it was recommended that the tumor be excised and the base thoroughly cauterized. The pedicle was snipped off with scissors, and the stump and adjacent tissues deeply frozen by means of Pusey's[5] solid carbon dioxide snow. As an antiseptic, a 1 per cent. aqueous solution of liquor cresol compositus was prescribed, and moist dressings, to be changed twice daily, ordered. It was not necessary to make a second application of the snow, as the wound healed quickly, and all dressings were dispensed with at the end of a fortnight. The excised lesion was fixed and hardened in alcohol, mounted in paraffin, and a number of sections made. For staining purposes, hematoxylin-eosin and polychrome methylene blue were used, with Unna's orcein for elastic fibers and Gram-Weigert for bacteria. The tumor consisted of a globular mass of connective tissue, so filled with dilated bloodvessels as to resemble an angioma. Near the base the covering was made up of irregular masses of swollen polygonal cells, but the greater part of the surface was so necrosed that the character of the component cells was not recognizable. The vessels were enormously dilated, and no signs of endothelial proliferation were present. The cavities were for the most part filled with blood. The intervascular stroma was infiltrated with leukocytes, and large numbers of mast cells also were present. No

[5] Jour. Amer. Med. Assoc., xliv, 1354.

giant cells were to be found. Throughout the growth were irregularly distributed collections of cocci, the number of organisms in each group varying from six or eight to several hundred. No peculiarity in grouping was to be noted, however, and nothing resembling the bodies described by Bollinger was observed. No glandular structures were to be seen.

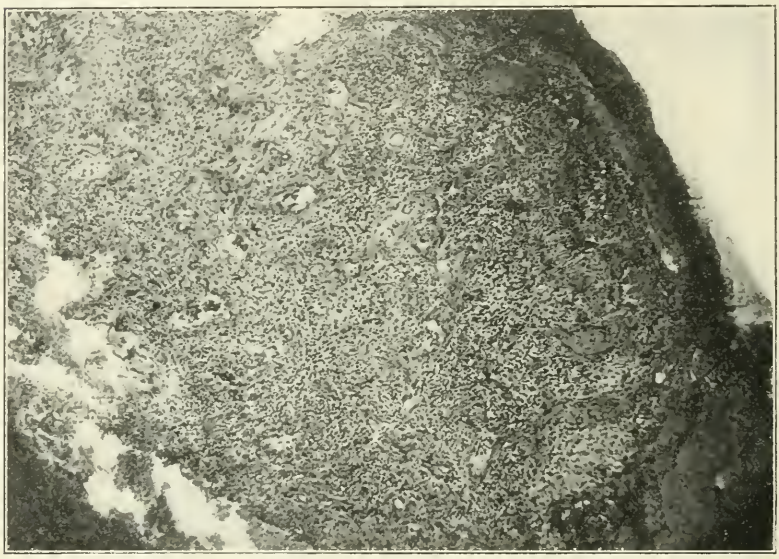

Fig. 3.—Dilated vessels in central portion of tumor, some filled with blood. (Zeiss, obj. C., no ocular.)

Animal Experimentation. For inoculation purposes, pus obtained directly from the lesion and staphylococci from the pure cultures on agar were employed. Two healthy adult guinea-pigs were used. A spot on each side of the animal's body was shaved, and the skin thoroughly cleansed with soap and water, followed by alcohol. Superficial lacerations were then made with the point of a knife, and the pus and cultures thoroughly rubbed in by means of a cotton swab on an applicator.

Guinea-pig A. Inoculated from lesion September 6, 1910. Thirty-six hours later the infected area had become red, glazed, and swollen, and on the right side several tiny pustules had developed. On culture it was found that these contained the aureus and a few Staphylococcus epidermidis albus. The left side healed completely within four days, and the area on the right within eight days.

Guinea-pig B. Inoculated from pure agar culture September 12, 1910. The skin was prepared three days previously, in order to secure the presence of an inflammatory condition at the time of

inoculation. Six loopfuls of bacteria and culture material were thoroughly rubbed into the injured integument. Several pustules formed in the course of seventy-two hours, and at the end of five days there was considerable crusting. Nothing that resembled the original lesion developed, however.

It is very probable that granuloma pyogenicum is the result of a staphylococcic infection of the upper corium, and that the involvement of the superficial structures is not directly concerned in its production. The irritation set up by the bacteria and their products gives rise to excessive cell proliferation, and the resulting granulation tissue is forced upward through the opening in the epidermis through which infection of the deeper tissues originally took place.

NOTE: Since this article was written, a valuable and exhaustive communication on the subject has been made by Udo J. Wile.[6]

GENERALIZED ERUPTIONS OF AN UNUSUAL TYPE, CAUSED BY THE ABSORPTION FROM A BELLADONNA PLASTER AND FROM THE OCULAR INSTILLATION OF ATROPINE.[1]

REVIEW OF THE LOCAL AND GENERAL ERUPTIONS CAUSED BY BELLADONNA AND ATROPINE.

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DERMATOLOGIST TO THE PRESBYTERIAN HOSPITAL; ASSISTANT IN DERMATOLOGY, UNIVERSITY OF PENNSYLVANIA; ASSISTANT DERMATOLOGIST TO THE PHILADELPHIA GENERAL HOSPITAL; DERMATOLOGIST TO THE CHURCH HOME FOR CHILDREN, TO THE BAPTIST ORPHANAGE, TO THE DISPENSARY OF THE CHILDREN'S HOSPITAL; ASSISTANT DERMATOLOGIST TO THE DISPENSARIES OF THE PENNSYLVANIA HOSPITAL AND THE HOWARD HOSPITAL, PHILADELPHIA.

THE subject of belladonna poisoning can, for the convenience of our study, be divided into the local and general eruptions caused by the internal administration of the drug; more or less generalized eruptions caused by the absorption from the local applications of the drug; general symptoms of poisoning, without an eruption, from the local absorption of the drug; local eruptions from the irritation of the local application of the drug; and general eruptions of unusual types from the internal administration or the absorption of the drug from external application.

[6] Unna's Festschrift, Leopold Voss, Hamburg, 1910, p. 333; also Jour. Cutan. Dis., 1910, p. 663.

[1] Read before the Northern Medical Association of Philadelphia, November 24, 1910.

Local and General Eruptions Caused by the Internal Administration of Belladonna. In reviewing the cases of eruption caused by the internal administration of belladonna, one is impressed by the fact that the great majority of the outbreaks are of the erythematous or scarlatinal types. Holthouse reported the case of his son, aged three years and eight months, who took by mistake two drams of a solution of atropine, two grains to the ounce. The skin shortly afterward became hot and dry, and covered with an intensely pruritic rash resembling scarlatina. McNab recorded a case in which a child while out at play ate some berries of belladonna, which was followed shortly afterward by congestion and swelling of the face. In a case reported by Woodman, a woman, aged twenty-one years, took internally, by mistake, a fluidounce of a solution of extract of belladonna rubbed up in water; her face and neck shortly afterward became scarlet. Meredith described a case in which a woman, aged between fifty and sixty years, took, accidentally, methylated belladonna liniment, the quantity being equivalent to twelve grains of camphor and one-half ounce of macerated belladonna root. A few minutes later a scarlet rash appeared on the neck, the upper part of the chest, the forearms, and the hands. Walmsley's patient, a child, aged three years, took four drops of tincture of belladonna; shortly afterward its face became flushed and covered with a scarlatinal blush, interspersed with white spots of irregular size, and shape. Sadler reported a case of idiosynerasy to the drug. An infant, aged three months, was given a teaspoonful of a mixture containing $\frac{1}{200}$ grain of atropine sulphate to a fluidram; a few minutes afterward the child's face and the upper half of its body became red; this continued for five hours. The same effect was produced with one-half of the dose and with even six drops, the latter being the equivalent, approximately, of $\frac{1}{800}$ grain of atropine sulphate; with the last dose, however, the redness lasted for only one-half hour. Nisbet's patient, a male, aged sixty-one years, took, by mistake, a fluidounce of belladonna liniment, with which was mixed 12 per cent. of chloroform liniment. Three hours later a punctate rash appeared over the chest, the abdomen, and the upper arms. Putnam stated that he had often seen an erythema appear on the face and the chest of babies, lasting about two hours, after even $\frac{1}{32}$ grain of the extract of belladonna had been given. Webber referred to a lady, aged forty years, who had an erythematous eruption on the cheeks after taking $\frac{1}{6}$ grain of extract of belladonna, three times a day, for a few days. Hutinel's patient, a girl, aged twenty-seven months, took fifteen grams of syrup of belladonna; shortly afterward she was attacked by a vivid scarlatinal eruption on the face and the upper part of the trunk. The eruption consisted of large red plaques presenting fine white points. There was very little itching. The eruption lasted for twelve hours, and then disappeared without

leaving a trace. The skin in Lusanna's case became bright red one-quarter of an hour after the administration of atropine, and persisted for one-half hour. The eruption was noted on the face, chiefly in the neighborhood of the ears, and on the hands. Jolly recorded a case in which a mistake was made in a purgative mixture, 44 grains of belladonna being placed in the preparation instead of that quantity of jalap. One hour after taking the mixture redness of the eyes and the face developed, which spread over the entire cutaneous surface, resembling markedly scarlatina. Berenguier reported a scarlatinal eruption on the face and the upper part of the trunk, in a girl, aged twenty-seven months; fifteen drops of the syrup of belladonna had been taken. In Gray's case, belladonna produced a diffuse scarlet efflorescence studded with innumerable papillæ resembling very closely the rash of scarlatina; the upper extremities and the trunk were attacked. In a case which came under Morrow's observation, a child, aged four years, was given an aperient pill containing $\frac{1}{4}$ grain of extract of belladonna. Two hours later there was an excessive flushing of the face, which shortly afterward extended over the body, giving an appearance resembling a "boiled lobster." The eruption disappeared in twenty-four hours, leaving no trace. Köbner observed a characteristic hyperemia of the face from the use of suppositories in the vagina, containing the extract of belladonna.

Eruptions Caused by Absorption from Application of Belladonna Plasters. Judd prescribed a belladonna plaster, about twenty-six inches square, for a strain of the left side and the back. Three hours later the patient's neck and face were flushed to a deep scarlet. Fleming's patient developed the symptoms of poisoning about twelve hours after the application of a belladonna plaster, five by eight inches in size. The plaster had been applied to an area previously inflamed by a strong liniment. The character of the rash on the trunk was not described. Morgan referred to a gentleman who developed a scarlet rash, general in distribution and accompanied by intense itching. A belladonna plaster, at least one foot square, had previously been applied to his loins for lumbago. Harrison's patient gave the history of having applied a belladonna plaster, which caused such irritation that it had been removed; another belladonna plaster was subsequently placed on the abraded area, causing a short time afterward a generalized eruption of a scarlatinal type. Caesar recorded a case in which a belladonna plaster produced an herpetic eruption from the local irritation of the application. Ten years later the same woman, aged thirty-two years, was ordered another belladonna plaster, the itching and burning keeping her awake all night. The whole left side of the trunk became covered by a vesicular eruption situated on an inflammatory base, which outbreak was limited by the median line of the back

and in the front and below by the crest of the ilium. Two days later a mixture of quinine and fifteen drops of tincture of belladonna was ordered, to be given three times daily; the following day a scarlatinal rash appeared on the face, the chest, and the arms. Quinine was given alone and the rash disappeared. Belladonna was then ingested, uncombined, and the eruption reappeared. In the case reported by Griffiths, a woman, aged twenty-three years, applied belladonna plasters to the breasts to "dry up the milk." After the plasters had been *in situ* for some days a well-marked pustular dermatitis was noted on the areas covered by the medication, and a rash of an urticarial type was observed on the arms, the forearms, the anterior surface of the knee-joints, the lower one-fifth of the thighs, and the upper one-fifth of the legs. There was considerable pruritus. Robert Brown referred to a case in which a belladonna plaster caused an inflammation of the skin, with serous discharge.

Poisoning, without an Eruption, Caused by the Application of Belladonna Plasters. In several reported cases the application of a belladonna plaster has given marked symptoms of poisoning, without the development of an eruption excepting, in certain cases, at the site of the plaster. Cases of this character have been reported by Desrosiers, Sym, T. J. Walker, Howarth, Taylor, Douglas W. Montgomery, Burrall, Tansley, Maddox, Clendinnen, and Jenner. In Pye-Smith's case, the advent of an eruption following the application of a belladonna plaster was not mentioned. Goodwin described a curious case in which a woman applied a belladonna plaster for an abscess of the breast, an opening being made in the plaster for the nipple. Her infant died suddenly after nursing at the breast covered with the belladonna plaster, whether from absorption of the belladonna through the mother's milk or from the plaster directly could not be determined. The mother had mild symptoms of poisoning.

Eruptions Caused by Absorption from the External Applications of Belladonna, Exclusive of Plasters. Le Gendre recorded a case in which a woman applied a mercurial preparation for pain in the mammary region, following the same with cataplasms impregnated with belladonna. There was a tremendous reaction, the skin of both breasts, the sternal region, the epigastrium, and the right axilla exhibiting an erysipelatous surface, in certain places ulcerating, with bleeding and suppuration, also vesicular and bullous formation. The axillary glands were enlarged. Fever and ptyalism developed. Six hours after the application of the pomade of mercury and belladonna the body became covered with an eruption resembling scarlatina. Spencer stated that he had treated a case in which a generalized scarlatiniform eruption followed the application, for twenty-four hours, of glycerinum belladonnæ to

the abdomen of a woman. Robinson reported an instance of unusual susceptibility to the local application of belladonna. A man while crushing the leaves and stems of fresh belladonna, accidentally splashed some of the juice on his face, hands, and arms; twenty-four hours later patches of erythema, vesicles, and pustules were scattered over the face. Two years later the man made up four dozen tablets of atropine; the following day his face was covered by an erythematous, vesicular, and crusted outbreak, resembling the dermatitis caused by fierce sunlight. There was marked pruritus. The application of a belladonna plaster, on another occasion, caused a localized vesicular eruption. J. G. Wilson recorded two instances of generalized scarlet efflorescences from the use of belladonna liniment on the breasts of two women, aged twenty-six and twenty-seven years respectively. The eruption appeared in each case on the fourth day after the liniment was first applied, and lasted for a few days after the medication was discontinued. Bloomfield ordered belladonna ointment for a swollen parotid gland, in a girl, aged twelve years; two hours after the second application of the preparation the face became scarlet. Owens describes a case, in a man, aged seventy-three years; a generalized erythematous eruption developed after six drops of a solution of atropine (2 grains to the ounce) had been instilled into the eyes.

Several other papers have been written on this phase of the subject which I have been unable to consult. Enwald and E. H. Brown have compiled articles on poisoning and the eruptions of the skin caused by the external applications of belladonna. Lyman has heading his article, "Poisoning from Belladonna Plaster." Poor takes up the question of skin idiosyncrasy to atropine. Magne has written on the extraordinary idiosyncrasy to the instillation of solution of atropine and belladonna into the eyes.

Poisoning, without an Eruption, from External Applications of Belladonna, Exclusive of Plasters. Several instances of this character have been reported, with more or less severe symptoms of poisoning. Symptoms are produced in the cases of R. G. Brown and Fraser by the external use of the liniment and a lotion containing belladonna. The derangement from the normal was caused in Cooper's patient by the application to the scrotum of an ointment containing belladonna and mercury.

Local Eruptions Caused by the Local Irritant Effect of Belladonna or Atropine. There will be considered under this heading those cases in which the drug itself acted as an irritant to the skin, the dermatitis being in no way caused by the absorption of the belladonna or atropine into the general system through the skin. Julius Donath related a case in which whenever atropine was instilled into the eye an erysipelatous redness developed on the face and the neck. The cheek, the neck, and the shoulder were

swollen, red, and covered with vesicles forming a continuous patch, indistinguishable from a acute vesicular eczema. In Chisholm's patient a strong solution of atropine caused the lids to become puffed and red, with an erysipelatous blush extending down the cheeks. A 1 per cent. solution of atropine sulphate caused circumscribed injection of the conjunctivæ, with swelling of the eyelids and the contiguous cheeks. Duboisia in this patient brought on temporary insanity. Following an instillation of atropine, in Wallace's case, the skin over the eyelids and upper part of the face was swollen, dark red in color, and of a tense, brawny feel; the eyes were closed by the swelling, and a profuse discharge came from the inner canthus. A local dermatitis had previously been produced in this same patient by the application of a belladonna plaster. Lawson stated that he had seen a dermatitis on the cheeks, from the irritant effect of the overflow of atropine from the eyes. Bryce instilled two to three drops of liquor atropii sulphatis (B. P., 1885) into the left eye of a patient, the overflow of the liquid and the tears causing a dermatitis of the cheek. Previous application of a belladonna plaster and belladonna liniment caused a local dermatitis. Mackintosh described an herpetic eruption developing from the local irritant effect of the drug. Belladonna liniment applied to a painful knee-joint caused the outbreak in the first instance, and a solution of atropine instilled into the eyes developed the exanthem on the cheeks, also swelling of the eyelids, on a second occasion. Fialkowski reported a case in which a solution of atropine used in the eyes produced, on the second day, an erythema and eczema of the eyelids. The atropine being continued for ten days, almost the entire face of the patient became covered by a confluent eczema. Liebreich has observed conjunctivitis, erythema, eczema, and pearly granulations of the conjunctivæ after the long-continued use of solutions of atropine, instilled into the eyes. Burdenell Carter has written that when atropine has been long in use, even the purest and most neutral solution is apt to cause local irritation in some individuals, and this irritation is usually more manifest in the eyelids, especially the lower, and on the adjacent cheek.

Local Idiosyncrasy to Atropine (Author's Case). Case I.—A negress, aged twenty-three years, came to the skin dispensary of the Pennsylvania Hospital in 1907, with an eruption involving the entire left cheek, the left side of the nose, and the left lower eyelid. The eruption consisted of innumerable miliary and larger vesicles on an acutely inflammatory base; there was considerable crusting, the latter being honey-colored. The left eye was closed by the marked swelling. There was considerable amount of itching, The eruption developed after the instillation of a solution of atropine into the eye. In October, 1909, the patient was again seen in the skin dispensary of the University of Pennsylvania Hospital,

with an acute vesicular eruption; almost the exact counterpart of that seen on the first occasion. The same history was again elicited. The eruption in the first instance lasted for six weeks and in the second attack for two weeks (Fig. 1).

Fig. 1.—Case I.

Unusual Eruptions Caused by the Internal Administration of Belladonna. Tardieu stated that occasionally petechial spots may be caused by the ingestion of belladonna. Boecke recorded an instance in which $\frac{1}{4}$ grain of extract of belladonna, ordered three times a day for a consumptive patient, after the second dose produced an erythema and partial gangrene of the skin of the scrotum. Crocker referred to a case, seen with Whipham, in which a man of forty years wore a belladonna plaster for a week and then took two 7-drop doses of tincture of belladonna. The next day the hands and the feet were swollen, red, and tense; the palms were deep red, with thickening of the epidermis; the soles were less affected; over the knuckles and all points of pressure the redness was intense, and capillary pulsation could be demonstrated by flexing the joint.

Dreyfous reported a case, of considerable interest, of a man, aged thirty-two years, with paralysis agitans; he was given belladonna in ascending doses; after 15 c.c. had been taken, which was followed by a vapor bath, intense itching developed, keeping the patient awake all night. On the next morning the patient's skin exhibited a somewhat generalized eruption. There was a diffuse vivid redness of the lower part of the face resembling erysipelas.

The eyelids were enormously swollen, and small vesicles were noted on the edges of this swelling. There were small nodules on the lobe of the right ear, and the left ear was swollen and red. The posterior portion of the neck, the external portion of the thighs, and the knees were scarlet. The eruption was of the type of the papular erythema on the extremities. There was a diffuse erythema in the neighborhood of the articulations of the elbows, more of a rose tint, but also slightly on the yellowish color. The skin on the dorsal surface of the forearms was dry, wrinkled, infiltrated, red, and formed of pinkish disseminated points; the surface was crusted from the desiccation and breaking of the vesicles. The skin at the bend of the elbows was moist and encircled by crusts and scales. There was a red sinuous line on the dorsal surface of the wrists. Irregularly shaped pinkish patches were found on the dorsal surface of the hands and the fingers, with intervening areas of sound skin. Small acuminate red points surmounted by a vesicle were noted on the back; in some places the eruption had run together, forming red, erythematous, disseminated large plaques. Patches of a light rose color were seen on the abdomen and the chest; these later plaques consisted of innumerable rose-tinted small points, giving the patch a uniform color. The anus was surrounded by large erythematous areas, with considerable crusting. The prepuce and the scrotum were edematous and very much swollen; the irritation caused frequent erections. No eruption was present on the lower portion of the cheeks, the chin, the nose, the palms of the hands, the shoulders, the legs, or the feet. The mouth was dry; the throat normal. The pulse and temperature were unaffected. The pupils were normal. Itching was intense. The eruption almost entirely cleared up in four days.

Gaucher, Boisseau, and Desmouliere reported an interesting case of idiosyncrasy to two separate drugs—hydrocyanic acid and belladonna. The patient was given for abdominal pains $\frac{7}{100}$ mg. of hydrocyanic acid; twelve hours later a vesicular eruption appeared which extended rapidly over the entire trunk and the upper part of the legs. This lasted for fifteen hours, and then disappeared without desquamation, with no general symptoms. Some time later the patient was ordered a mixture; he took the first dose, containing 5 drops of cherry-laurel water and 4 grams of syrup of belladonna in the evening; during the night a generalized urticarial eruption appeared. The skin was edematous, violet in color, intensely itchy. Desquamation started about midday, becoming generalized; large scales of epidermis fell off, continuing for four days. Ten days later a mixture was given for bronchitis, in which syrup of belladonna was prescribed without the cherry-laurel water; twelve hours later a new pruritic eruption appeared, analagous to the preceding, without consecutive desquamation. Two medicines were, therefore, causal in this case, each having been given sep-

arately, with the same result. The sediment of the urine examined under the microscope showed the presence of numerous crystals of cystine; chemical tests proved the same. The authors consider that this, therefore, was the cause of the patient's idiosyncrasy to the drugs. The presence of cystine crystals showed a derangement of nutrition, an insufficient amount of oxidation, and an abnormal intestinal fermentation. The patient was profoundly shocked by this derangement of nutrition, thus causing the susceptibility to the drugs.

Fallen gives the details of a case in which a somewhat generalized scarlatiniform and eczematous eruption was produced by the ingestion of a combination of opium and belladonna. The eruption was reproduced by giving opium alone. As the belladonna was not administered uncombined, it cannot be positively stated that this drug would have produced any eruption or an outbreak of this type.

Generalized Eruptions, of an Unusual Type, Caused by the Application of a Belladonna Plaster and the Instillation of Atropine (Author's Cases). Case II.—Joseph P., born in Greece, well-built, aged twenty-five years, came to the skin dispensary of the Pennsylvania Hospital March 29, 1909. The patient led an active outdoor life, peddling various commodities in a wagon. He complained that an intensely itchy eruption had appeared three days previously. A generalized eruption was noted on the removal of the clothing, and two large belladonna plasters were found over the scapular region. The history was elicited that eight days before his visit to the dispensary the two plasters had been applied because of a slight cough; five days later the rash appeared; at the time of appearance it was of a bright red color, and very itchy. The patient had had no bowel movement for ten days; he stated that his usual habit was to go but once each week. The skin was dry and hot. The patient complained of having a dry mouth and throat, and being very thirsty. The pupils were only slightly enlarged, reacting somewhat sluggishly to light. The temperature, pulse, and respirations were normal. The face was flushed. Dark red erythematous spots covered almost one-half of the anterior portion of the chest, becoming confluent on the lateral portions. Large dark red areas involved the axillæ; reddish plaques, with a tendency to confluence, involved the anterior and posterior portions of the upper arms and the forearms. Irregularly shaped dark red patches, with intervening sound skin, were found on the dorsal surface of the hands. There was a continuous sheet of eruption extending over the abdomen, the groins, the thighs, and the legs to the knees, of a violet-red color, with a tendency to form areas resembling purpura, but from which most of the color could be pressed (Fig. 2). The upper part of the back exhibited dark red patches, with intervening sound skin, from a dime to half a dollar in size. There was a continuous reddish-violet colored plaque, extending from the lumbar region to

the popliteal spaces (Fig. 3). The lower legs, anteriorly and posteriorly, showed only scattered patches, mostly dime-size or smaller, irregularly round, of a bluish color. At the time of the patient's visit, two days later, the plaster having been removed, the eruption had faded considerably, exfoliation had, however, commenced. Exfoliation was marked on the anterior and the posterior axillary folds, the lower abdomen, the back, the inner surface of the thighs, and the upper legs; it occurred in small flakes and strips. On the

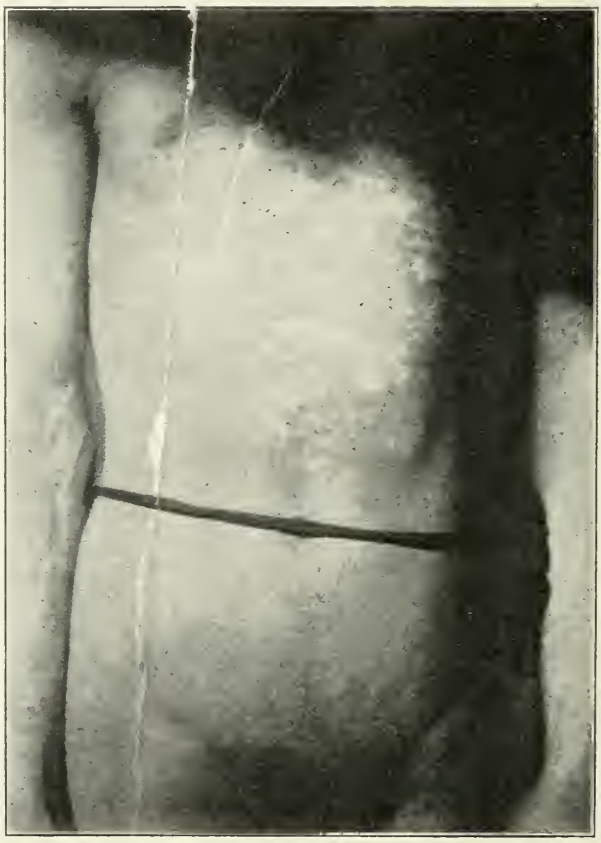

Fig. 2.—Case II. Anterior aspect.

third visit, a few days later, the eruption had almost disappeared, the exfoliation had stopped, but there was some pigmentation where the former outbreak had been.

Case III.—John O., bricklayer, born in Italy, aged thirty years, came to the skin dispensary of the Pennsylvania Hospital August 18, 1909, complaining of a pruritic eruption of three days' duration. A generalized outbreak was present, consisting of bright to dark

red, erythematous, macular spots, which had become confluent on the chest, the lateral portions of the trunk, the outer surface of the arms, and the thighs. The macular lesions varied from a split pea to a silver dollar in size. The eruption was scanty on the forearms and lower portion of the legs. The hands and the feet were not attacked. The lesions on the lower portion of the trunk, the buttocks, and the thighs were bluish red, of a darker color than those on the upper part of the body. The face exhibited an eruption of a

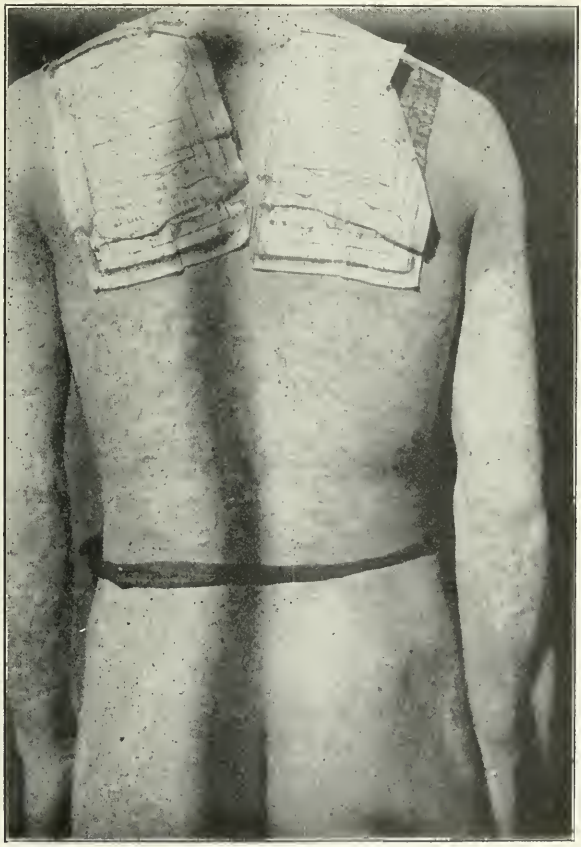

FIG. 3.—Case II. Posterior aspect.

like character, but fainter and of a pinkish color. According to the history, two weeks previous to the appearance of the outbreak, the cornea of the right eye had been injured by a foreign body, just to the right of the pupil, and four drops of atropine had been instilled daily, for a few days. The patient, on his own initiative, had continued this treatment until the appearance of the present eruption. The prescription contained atropine sulphate, 0.15 gram; cocaine

hydrochlorate, 0.3 gram; distilled water, 10 grams. An eye lotion had also been given, containing boric acid, biborate of soda, and water. The pupil of the right eye, into which the solution of atropine had been instilled, was widely dilated. The left eye, into which no drops had been placed, was also somewhat dilated. The throat and mouth, according to the patient, were very dry. The pulse, the temperature, and the respirations were normal. The patient stated that he had been constipated since instilling the atropine.

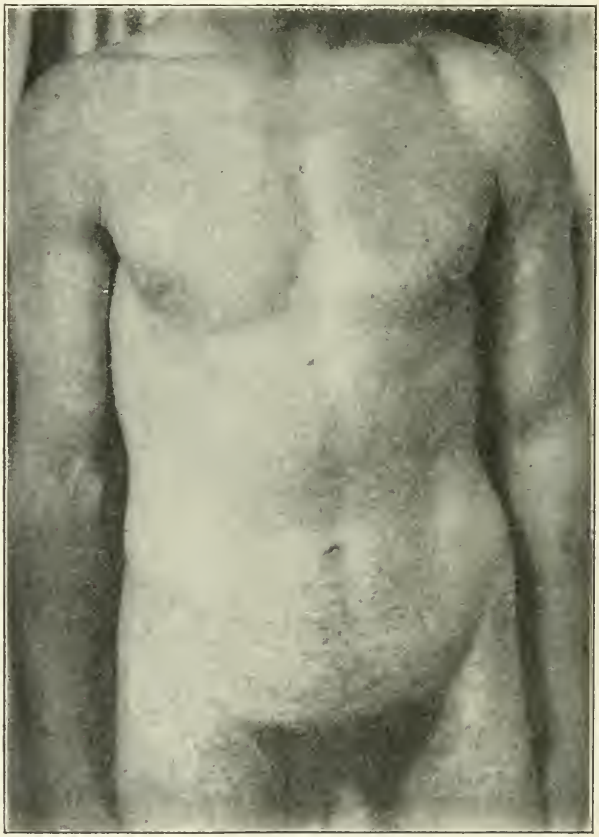

Fig. 4.—Case III. Anterior aspect.

Various symptoms of poisoning were noticed in the great majority of the reported cases, muttering delirium, incoherence in speech, rigidity of the limbs, convulsions, twitching of the muscles, giddiness, staggering gait, delusions in regard to imaginary people and things, cerebral excitement, delirium of laughing and violent types, constant desire to urinate, irritation of the entire urinary tract, rapid pulse, hurried and also deep breathing, hyperesthesia, and hyper-

pyrexia. Mild symptoms of poisoning were noted in the cases of Jenner, Sym, Walmsley, and J. G. Wilson, from the external application of the drug, and consisted of dryness of the mouth, tongue, and throat. Practically no symptoms of general poisoning were noted in the patients of Robinson, Putnam, Webber, Herbert Spencer, and Le Gendre. There was but one fatal case in this series, McNab's patient, a child, aged four years, who died seventeen hours after eating belladonna berries. The temperature reached 110°, a few hours before death.

Although in the great majority of the cases of belladonna poisoning, particularly those of the severe type, the pupils were widely dilated, in some there was only slight dilatation, and in a few there was no mydriasis. In two cases of poisoning, Walmsley's and Sadler's, in which the drug had been administered internally, the pupils were not dilated. Douglas W. Montgomery described a case in which the symptoms of poisoning, from a belladonna plaster, were very severe, but the pupils were absolutely normal. The pupils were also undilated in the cases of Law and Herbert Spencer, the poisoning being caused in the one case by absorption from a belladonna plaster and the other by the local application of belladonna glycerin. The eruption caused by the belladonna plaster in Caesar's patient was unaccompanied by mydriasis. In the cases of poisoning from belladonna plasters reported by Clendinnen and Maddox the pupils were only moderately dilated. In the author's case of belladonna plaster poisoning there was but slight dilatation of the pupils, and the pupil of the eye into which the atropine had not been instilled, in the third case, was only moderately dilated.

The one-sided action of belladonna is a curious phenomenon noted in a few reported cases. Burrall recorded a case in which a woman applied a belladonna plaster upon her right side, causing on the following day mydriasis on the right eye, the pupil of the left eye being absolutely normal. Tansley described two cases of this character: The first patient instilled a solution of atropine sulphate (4 grains to the ounce), once daily, into one ear for tinnitus aurium; twelve days later the pupil of the eye, on the same side as the instillation, became markedly enlarged; the other pupil remained normal. In the second instance, a patient applied a belladonna plaster for pain in the right side, four or five days later the right pupil became enlarged; the left remained undilated. J. Newton Smith mentioned his own case: He took $\frac{1}{2}$ grain of alcoholic extract of belladonna, three times daily; on the second day the right pupil became enlarged; the left was unchanged.

Accidentally a very small quantity of the vomited material got into Holthouse's eye; his son, at that time, was suffering from belladonna poisoning; a short time afterward the pupil became enlarged. The urine and the feces of the child were examined and dilated the

pupils of a white mouse's eyes. The vomited material also caused mydriasis of the eyes of a white mouse.

There is always a hesitancy in describing a unique, or at least an unusual, type of eruption, but the author considers that he is justified in ascribing the two generalized cases to the absorption of belladonna in the one case and of atropine in the other. One could hardly explain the occurrence of two eruptions of almost the same type, excepting that one was much more severe and was followed by exfoliation, on any other theory but that the same drug, or its alkaloid, used in each was causal of the outbreak. There is great regret on the part of the writer that the patients did not return, as directed, so that belladonna could have been administered again to conclusively prove the diagnosis.

Conclusions. 1. More or less generalized eruptions not only occur from the internal administration of belladonna or its alkaloid, atropine, but also from absorption through the skin of local applications of the same.

2. The skin does not have to be broken or denuded of epidermis for absorption to take place; the symptoms of poisoning, however, develop much sooner if such is the case.

3. The great majority of the cases exhibit an erythematous or scarlatinal type of eruption, which is more frequently found on the face and the upper portion of the body, but in a fair number of cases the outbreak is generalized. Gangrenous, purpuric, and eczematous eruptions have been reported. The author describes a unique, or at least a very unusual, type of outbreak.

4. Although in a great many instances severe symptoms of poisoning are present, the eruption may be unaccompanied by other manifestations of drug absorption.

5. Mydriasis is a quite constant phenomenon; in a few cases, however, the pupils were only slightly enlarged, entirely normal, or unilaterally dilated.

6. The prognosis is favorable; only one death occurred in this large series of cases.

7. Belladonna or atropine may produce a local eruption from the local irritant effect.

I wish to express my thanks to Dr. Charles N. Davis for the privilege of reporting these cases.

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INVESTIGATIONS CONCERNING THE VALUE OF THE MICROSCOPIC EXAMINATION OF THE BLOOD FOR BACTERIA.[1]

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The following investigation was undertaken at the suggestion of Dr. Libman, to determine, if possible, in what percentage of cases in which blood cultures were positive, bacteria could be found by direct microscopic examination, and also to determine whether organisms were present microscopically in cases in which blood cultures were negative. Altogether 250 cases were studied. The method followed was a combination of those used by previous investigators.[2] We used from 1 to 2 c.c. of blood, which was obtained at the same time that the blood was drawn for cultural purposes, and poured it into 20 c.c. of sterile 1 per cent. aqueous solution of sodium citrate, thus preventing coagulation. The citrate solution as well as all the stains and fluids that were used were passed through a Berkefeld filter in order to remove all contaminating bacteria and granules. The blood was then centrifuged for at least a half hour, and a few drops of the sediment were drawn up into a sterile pipette and deposited on from two to three chemically clean slides. The latter were kept in alcohol until within a few minutes before they were used. The smears were then made and fixed by heat. The blood was then laked with sterile filtered water, after which a 1 per cent. solution of acetic acid was poured over the slides to complete the laking. This was washed off and followed by a routine Gram stain. Various other stains—Giemsa, Unna's alkaline methylene blue, Loeffler's methylene blue, Jenner, fuchsin, and methyl-green-pyronin—were tried, but we found that the Gram stain gave the clearest fields for examination. From one-half to two hours were spent in examining each specimen.

Our method gave better results than that used by Staeubli, viz., collecting the blood directly in 3 per cent. acetic acid, because the fibrin in the sediment interfered with the clearness of the microscopic pictures.

[1] Read before the Section of Internal Medicine, New York Academy of Medicine, November 15, 1910.

[2] Staeubli, Beiträge zum Nachweis v. Parasiten in Blut, Münchener med. Woch., 1908, vol. ii; Rosenberger, The Presence of Tubercle Bacilli in the Circulating Blood, Amer. Jour. Med. Sci., February, 1909.

In cases in which the blood cultures showed the presence of Gram positive cocci, we could, with very few exceptions, and without any knowledge of the result of the blood culture, demonstrate the presence of the organisms within from one to two hours after the blood was withdrawn. By referring to the table, it will be seen that in 97 per cent. of the cases in which the blood cultures were positive, the blood smears were also positive. Frequently the number of bacteria seen on the slide was evidently larger than the number found culturally.

In 12 cases (see appended lists) bacteria were found on the slides although the cultures remained sterile. Of these ,5 were cases of lobar pneumonia, in which one might well expect to find bacteria in the circulating blood. In these smears the cocci which were found appeared as typical lanceolate diplococci. In one case of thrombosis of the lateral sinus the culture remained sterile, but numerous Gram-positive cocci were found on the slides. We might also mention that in 2 cases of acute articular rheumatism organisms resembling streptococci were found in the smears. The only explanation we can offer for negative cultural findings is either inadequacy of methods or devitalization of the organisms due to the bactericidal power of the blood. The results in the cases of rheumatism can be accepted only if confirmed in a large series of cases.

A series of experiments was tried on rabbits in order to obtain comparative results between cultures and spreads. By inoculating rabbits intravenously with varying quantities of cocci we attempted to determine:

1. The maximum length of time after inoculation at which the organisms could still be demonstrated in the blood.

2. The relationship between the number of colonies to 1 c.c. of blood in agar plates, and the number of bacteria found in spreads microscopically.

Experiment 1. Rabbit. Intravenous injection of 2,000,000,000 Staphylococcus aureus (counted by the Wright method).

After thirty minutes, 8 c.c. of blood aspirated from heart, 4 c.c plated, 2 c.c. in each agar plate, and 4 c.c. collected in sodium citrate solution. Result: Forty colonies to 1 c.c. of blood were counted in the plates after twenty-four hours, and numerous cocci were found easily in the smears.

After twenty-four hours, 5 c.c. of blood were aspirated, 3 c.c. were plated, and 2 c.c. collected in citrate. Result: 1 colony to 1 c.c of blood on the plates, and many cocci found easily in spreads.

After forty-eight hours, 10 c.c. of blood aspirated, 5 c.c. plated, and 5 c.c. collected in citrate. Result: Plates and spreads negative.

After seventy-two hours, animal killed. Cultures from liver and kidney showed Staphylococcus aureus, those from the glands and bone-marrow were negative. The sections showed multiple

abscesses in the kidney with numerous Gram-positive cocci, also a moderate number of cocci in the liver capillaries.

Experiment 2. Rabbit. Intravenous injection of 1,000,000,000 staphylococci.

After ten minutes, 4 c.c. of blood aspirated from heart, 2 c.c. plated, and 2 c.c. collected in citrate. Result: 350 colonies to 1 c.c. of blood in the plates, and many cocci found easily in spreads. Animal died after aspiration. Postmortem examination negative.

Experiment 3. Rabbit. Intravenous injection of 2,500,000 streptococci.

After fifteen hours, 5 c.c. of blood aspirated from heart, 3 c.c. of blood plated, 1.5 c.c. in an agar plate, and 1.5 c.c. in a plate of 2 per cent. glucose-agar; 2. c.c. collected in citrate. Result: Plates sterile. A few diplococci found in spreads.

Experiment 4. Rabbit. Intravenous injection of 35,000,000 staphylococci.

After fifteen minutes, 4 c.c. aspirated from heart, 2 c.c. of blood plated, and 2 c.c. collected in citrate. Result: Eight colonies to 1 c.c. on plates, and cocci found easily in spreads.

From these experiments we conclude that:

1. Bacteria can be found in the spreads when the cultures remain sterile (see Experiment 3).

2. The number of bacteria seen on slides was greater than the number of colonies grown on the plates (see Experiment 1).

3. Many more bacteria circulate in the blood than can be grown culturally, or seen microscopically.

The morphology of the bacteria as seen in the spreads was not always distinctive, but, as a rule, the streptococci were smaller than the staphylococci, and were seen to occur in diplococcus forms, rarely in chains. The staphylococcus appeared singly or in clumps. Identification of the organisms was verified by careful study of the blood cultures.

List I.—Cases with Positive Blood Cultures.

(*a*) *Streptococcemia.*

Diagnosis.	No. of cases.	Positive results in spreads
Bacterial endocarditis	5	4
Sinus thrombosis	2	2
Pyarthrosis	5	5
Osteomyelitis	5	5
Erysipelas	1	1
Postabortive general infection	4	4
Cellulitis of hand	1	1
Pneumonia; pericarditis	1	1
Pyopneumothorax	2	2
Total	26	25

(b) Staphylococcemia.

Meningitis	1	1
Osteomyelitis	4	4
Infected hemorrhoids	1	1
Pyelonephritis	1	1
Total	7	7

List II.—Miscellaneous Cases with Positive Findings in Spreads and Negative Blood Cultures.

Diagnosis.	No. of cases.
Lobar pneumonia	5
Sinus thrombosis	1
Acute articular rheumatism	2
Postpartum general infection	2
Epidural abscess	1
Liver abscess	1
Total	12

List III.—Cases with Negative Blood Cultures and Negative Microscopic Findings.

Diagnosis.	No. of cases.
Local infections	30
Appendicitis	8
Mastoiditis	8
Sinus thrombosis (?) mastoiditis	2
Otitis media	1
Puerperal infection	18
Peritonitis	2
Liver abscess	5
Cholecystitis	3
Pyelitis	1
Erysipelas	1
Chronic endocarditis	25
Brill's disease	5
Influenza (unreliable on account of Gram-negative rods)	3
Acute articular rheumatism	4
Gonorrheal arthritis	2
Leukemia	2
Total	120

Besides the cases already discussed, we studied 53 cases of typhoid fever. The method which we employed was found to be useless for this purpose, as Gram negative rods were found not only in the blood of cases of typhoid fever, but also in a large majority of spreads made from the blood of culturally positive streptococcic and staphylococcic cases, and also from the spreads made from many of the cases in which there was no bacteriemia. We can offer no explanation for the presence of these rods, unless possibly that they are hemokonia. We therefore tried to find typhoid bacilli with the ultramicroscope by examining a drop of the sedimented blood, pressing the same between a coverglass and a slide. The method proved to be impracticable on account of the difficulty of distinguishing the bacteria from hemokonia.

In some cases we poured the greater part of the sediment into a tube of bouillon, and placed it in the thermostat for from five to seven hours. The bouillon culture was then centrifuged, and slides were stained for microscopic examination. The number of Gram-negative bacilli in these cases, which were positive culturally, was so large that one could not mistake them for the Gram negative rods seen in small numbers in cases that were not instances of typhoid fever.

In this connection it is evident that because of the presence of Gram-negative rods the method used by us would be impracticable in examining the blood of any case in which the presence of Gram-negative bacilli was suspected. This would, of course, include cases of influenza, and, in view of our findings, we are unable to accept the results published by Canon.

Conclusions. The studies which we have here outlined will be continued in the laboratory to see if further data can be obtained. At the present time we can draw the following conclusions:

1. Bacteria can be found microscopically in the blood of the large majority (97 per cent.) of cases in which their presence has been demonstrated by blood culture.

2. In a number of the cases (12 in 132, about 9 per cent.)[3] bacteria were demonstrated in the blood which had been found sterile by means of blood cultures taken according to the methods now in vogue in our laboratory. Further studies must be made to determine whether there is any error in our findings.

3. It is probable that in cases of sinus thrombosis and in cases of osteomyelitis, microscopic examination of the blood may be of service in coming to a more rapid conclusion as to the presence of a bacteriemia.

4. Unless all possible precautions are followed in regard to asepsis, and unless all fluids and stains are filtered, the method is unreliable.

5. Microscopic examination of the blood with all the methods that have so far been used is not of service in cases in which the presence of Gram-negative organisms is suspected.

6. Microscopic examination of sedimented bouillon cultures may be of value in making an earlier diagnosis in some cases of typhoid fever.

[3]This includes all the cases with negative blood cultures except the cases of typhoid fever.

DIGESTION IN FEVER.[1]

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From time immemorial it has been quite universally believed that during fever the digestive powers of the system are very greatly impaired, if not altogether abolished. In the standard medical literature of all ages, from Hippocrates to the present time, this doctrine is either explicitly stated or implicity conveyed. The belief has had a profound influence on medical practice, being one of the influential considerations leading to the low dietary regimen that has in all times almost universally prevailed in the treatment of acute diseases.

Although this belief still has a strong hold and strongly influences medical practice, it will, perhaps, not be unprofitable critically to consider its basis and validity, and to attempt to determine the exact condition and extent of the digestive processes and powers during fever.

On a general view, it seems almost self-evident that in such a profound disturbance of the body functions as occurs in fever, digestion must necessarily be enormously lowered. Such a belief accorded well with the views as to the nature of the febrile process that dominated medical thought throughout most of medical history. So plausible, indeed, is this belief, from the general conditions present in many cases of fever, that it is quite natural that it should have become a settled conviction; and strong evidence may justly be demanded to shake or modify it. Nevertheless, such a basis for this doctrine can be characterized only as a deductive generality, whose validity to be maintained must stand the test of a scientific and logical critique.

Clinical and general experience may be appealed to in support of the view of abolished digestion in fever. On its face this seems a consideration of the utmost weight, yet, as Hippocrates said, "experience is fallacious and judgment difficult," and the history of medicine shows that the appeal to the results of experience is an argument to be accepted with great caution. Many theories and systems and methods of practice for a time have enjoyed universal approval and claimed justification on the basis of general experience, which nevertheless in the end were found erroneous and were utterly discredited. Preconceived opinions are apt to interfere with unbiassed interpretation of results; and the occurrence of disturbed conditions in a few cases is apt to impress the

[1] Read before the Medical Society of the District of Columbia, October 19, 1910.

mind unduly, so that conditions that are really exceptional are taken to be the rule.

The usual occurrence of anorexia in fever is commonly regarded as a reason for withholding food. It should be noted, however, that loss of appetite does not necessarily imply loss of digestive power. Experiments with absolutely unpalatable and untempting diets (such as ash-free diets) have shown that such food is digested as completely as ordinary appetizing food (Pavlov's teachings to the contrary notwithstanding).

The dry mouth and tongue in many febrile cases have naturally suggested a diminution or suppression of salivary secretion and digestion in fever.

Numerous investigations of gastric digestion during fever have been made.

Beaumont from his classical researches (1833) claimed that in the "febrile diathesis" very little or no gastric juice is secreted and digestion is much impaired; the conceptions of fever at that time, however, were very vague, and it would appear from his protocols that his subject did not at any time during the experiments suffer from real fever, but only from transient attacks of acute indigestion.

Investigations by modern methods (*i. e.*, the stomach tube) have shown that in the various fevers there is usually a diminution or total suppression of hydrochloric acid in the gastric juice, while the pepsin is apparently but little reduced. Gastric absorption has been found materially retarded in fevers, while von Noorden found the motor functions of the stomach little impaired.

Special studies of pancreatic and intestinal digestion in fever have naturally not been made, owing to the inaccessibility of these regions to investigation.

Inasmuch as the bulk of digestion is carried on by the pancreatic and intestinal secretions, concerning which we have no specific data, it is apparent that the observations at hand indicating some lowering of gastric secretion are not sufficient basis for any reliable judgment as to the total impairment of digestion in fever.

Fortunately we have at command a simple, accurate, and conclusive means of determining the exact degree of the total net digestion and absorption of the various foodstuffs in patients with fever—the same standard method by which the quantitative digestion of food in health is determined—a method available and easily applicable for any subject. This consists in making exact determinations of the food materials (protein, fat, carbohydrate) ingested during a certain period, and also of these same materials as discharged in the feces for the same period. The difference between the material ingested and that dejected necessarily represents the amount digested and absorbed. The estimation of protein is based on a determination of the total nitrogen (Kjeldahl method)

in the food and feces, that of fat on the material extractible by ether. As a certain though indeterminate portion of the nitrogen and ether extract in the feces is derived from excretions into the alimentary canal, desquamated epithelium, bacteria, etc. (and not from the food), the digestion is always more complete than the figures indicate. The error thus introduced is of considerable magnitude with small diets, and should be discounted in interpreting such, but with ample diets is of smaller moment and does not vitiate the method for purposes of comparison.

In order to form an exact estimate of the degree of impairment of digestion during fever by this method, I have collected all the reports of analyses of food and feces in febrile diseases which I could find published. These cover 155 cases (1386 days of observation in all) in which determinations of nitrogen (protein) in food and feces were made, and 31 cases (154 days of observation) in which fat determinations were made. These estimations were made by thirty-six different investigators for various purposes. Practically no determinations of carbohydrate were found, and consequently there are no data on which to base a specific judgment as to its digestibility; but carbohydrate is usually digested much more completely than protein or fat, and it is highly probable that in fever the falling off in its digestion is no greater (and is probably less) than that of protein or fat. While there is ample room for further investigation, the data thus collected are sufficient for the formation of at least a tentative estimate of the impairment of digestion and absorption of protein and fat during fever.

The data are presented in the two accompanying tables, giving the general daily averages in food and feces during actual pyrexia of protein (nitrogen) and fat respectively. The actual diets in the various cases varied greatly both as to the amounts and the kinds of food used; many of the patients were on diets consisting largely or exclusively of milk, while many received a well-mixed diet. On account of the large error with small diets, cases in which the daily nitrogen intake was less than 5 grams have for the most part (except in children) been excluded from the compilation.

General Averages per Diem of Determinations of Digestion and Absorption of Protein (Nitrogen) During Periods of Fever in Various Diseases.

Disease.	Number of observers.	Number of cases studied.	Number of days of observation.	Nitrogen in food, daily average. Grams.	Nitrogen in feces, daily average. Grams.	Percentage of food protein (nitrogen) absorbed.
Typhoid fever	20	71	716	11.7	1.9	83.6
Typhus fever	2	15	84	9.9	1.4	85.7
Relapsing fever	1	1	6	7.6	1.1	86.2
Tuberculosis, pulmonary	11	33	323	21.0	2.6	88.3
"Chronic pneumonia" (probably including cases of phthisis)	3	6	79	11.8	1.4	87.8
Acute pneumonia	4	20	103	10.2	1.4	86.1
Acute pleuritis	2	2	14	9.8	1.9	80.6
Suppurative pyelonephritis	1	1	17	19.1	1.7	91.1
Scarlatina	1	6	44	5.3	0.6	88.6
Totals and general averages (by cases)	35	155	1386	13.3	1.9	86.0
Cases on exclusive milk diet		32	165	10.5	1.4	86.5

General Averages per Diem of Determinations of Digestion of Fat During Periods of Fever in Various Diseases.

Disease	Number of observers	Number of cases studied.	Number of days of observation.	Fat in food, daily average. Grams.	Fat in feces, daily average. Grams.	Percentage of food fat absorbed.
Typhoid fever	3	16	91	59.3	5.0	91.6
Typhus fever	1	4	18	23.4	3.9	83.2
Relapsing fever	1	2	8	25.8	4.4	83.1
Intermittent fever	1	1	6	19.4	2.6	86.6
Erysipelas	1	2	6	36.0	7.5	79.3
Tuberculosis, pulmonary	3	3	14	59.5	4.8	91.9
Acute pneumonia	1	2	8	22.3	4.7	78.9
Varioloid	1	1	3	43.4	5.7	86.9
Totals and general averages (by cases)	6	31	154	46.8	4.9	89.6
Cases on exclusive milk diet	2	22	84	38.4	4.6	88.0
Cases on diet of egg yolks	1	2	8	128.0	7.5	94.2
Cases on diet of ham	1	3	11	12.5	3.4	72.8
Cases on diet of porridge	1	2	8	84.0	7.1	91.6
Cases on mixed diet	5	8	43	73.9	6.0	91.9

For purposes of comparison the percentages of digestibility of the several foodstuffs in health, as determined by Atwater, may be stated, as follows:

	Protein.	Fat.	Carbohydrate.
Animal food	97	95	98
Vegetable food	84	90	97
Mixed diet	92	95	97

Examination of the figures in the tables shows for protein a general average digestion in fever of 86 per cent. in 155 cases of nine different diseases; this is a falling-off from the normal digestion of 11 per cent. if compared with animal food, or of 6 per cent. if compared with mixed diet, but is 2 per cent. better than the digestion of protein in vegetable food in health.

For fat, the general average digestion in fever in 31 cases of eight different diseases was 89.6 per cent., a falling off from health of 5.4 per cent. as compared with animal or mixed diet, and practically the same as the digestion of vegetable fat in health.

The determinations show no tendency for a lower degree of digestibility with the larger diets. In the typhoid fever cases, for example, the digestion and absorption of the food protein with varying amounts of protein in the daily ration was as follows:

Daily amount of protein in food.	Percentage of food protein absorbed.
Under 25 grams	57.9
25 to 49.9 grams	74.2
50 to 74.9 "	86.0
75 to 99.9 "	86.0
100 to 124.9 "	88.1
125 to 149.9 "	85.0
150 to 174.9 "	88.1
Over 175 grams	84.0

The cases on exclusive milk diet show a digestion of protein only 0.5 per cent. higher than the average, while that of fat is even less than the average. This showing does not support the prevalent belief in the superior digestibility of milk during fever.

In general, so far as shown by the data available, the average reduction of digestion during fever ranges not over 5 to 10 per cent. This falling off is so small as for practical purposes to be almost negligible; indeed, the digestion of animal and mixed food in fever is quite as good as that of vegetable food in health. The belief in a great impairment of digestion in fever is an idea based on vague impressions and dogmatic assumptions that has come down to us from the dark ages of medicine. The reduction actually shown by exact observations is so small as to dispel any fear, in general, of fever patients being unable to digest and absorb an adequate amount of the nutriment offered them, or to necessitate on that account any diminution of the diet.

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HEMORRHAGES OCCURRING WITHIN A BRIEF PERIOD IN A GROUP OF CASES OF PULMONARY TUBERCULOSIS.*

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The rarity with which detailed reports have been published of hemorrhages in groups of cases of tuberculosis, and some features of special interest in the series herewith presented, are the occasion for the present report.

The outbreak occurred at the Home for Consumptives, at Chestnut Hill, Philadelphia, in which there were at the time 66 patients, 10 being incipient cases, 11 moderately advanced, and 45 far advanced. About one-fourth were males and three-

* Read before the Section on Medicine, College of Physicians of Philadelphia, November 28, 1910.

fourths females. Over one-half were between twenty and forty years of age. These figures, except that the total number of cases is a little low, correspond closely to the daily average at the Home. During the whole year 135 cases of pulmonary tuberculosis were under treatment, and during this time 43, or about one-third, expectorated blood at one time or another. The numbers expectorating blood each month were 11 in May, 15 in October, and in the remaining months varied from 2 in February to 9 in December. The longest period of absence from hemorrhage was sixteen days, from May 20 to June 4. There were two periods in which the hemorrhagic cases were concentrated, one from April 21 to May 19, in which 12 cases spat blood, and the period under consideration.

A glance at the table shows that in the brief period of three weeks, from September 30 to October 20, there were 14 individual cases expectorating blood, or between one-fifth and one-sixth of all the patients in the Home at the time, and about one-third of all the patients who expectorated blood throughout the entire year. On only one day of this period was there no patient spitting blood. During the previous three weeks only 4 cases and during the subsequent three weeks only 2 cases had hemorrhages. This is a large proportion of cases, even when compared to the frequency of hemorrhages in all cases of tuberculosis. This frequency varies, according to different statistics, from about one-fourth to over four-fifths of all cases, depending on the class of cases and the time they are under observation.

The patients at the Home are distributed pretty equally in four separate buildings, which are united by enclosed passages, and the number of hemorrhagic cases in this series was about equal in each building.

All of these 14 cases had expectorated blood at some time previously, but a considerable period had intervened in most of them, over three months in 5 of the cases; 1 incipient case was admitted during the outbreak and expectorated blood for the first time in a month.

The first case to develop hemoptysis during this outbreak was quite subject to hemorrhages. She had had streaky sputum a month before, and again two days before the first date given in the table, when she had a hemorrhage of eight ounces. Every day or two following for three weeks some new case would spit blood.

Besides the number of hemorrhagic cases in this series their severity is noteworthy; 6 of the 14 raised pure unmixed blood, and of these, 3 died immediately from the effects of the hemorrhage and a fourth expectorated twenty-four ounces of blood and died twenty-five days later without any recurrence of the hemorrhage. During the whole year 31 cases at the Home terminated fatally. Anders[1] records only 10 immediately fatal cases of hemorrhage out of 5302 cases. West[2] estimates that 1 to 2 per cent. of all deaths in phthisis are due to fatal hemorrhages.

No.	Sex.	Age.	Stage.	Condition prior to hemorrhage.	Sept. 30	Oct. 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
116	F.	23	F. A.	Progressive	8 oz.	..	..	5 oz.[1]																	
48	F.	29	F. A.	Stationary	..	B.S.	..	..	..	..	..	..	..	..	..	B.S.									
95	M.	46	F. A.	Progressive	..	B.S.																			
135	F.	18	F. A.	Improved	..	..	24 oz.[2]																		
160	M.	21	F. A.	Improved	..	..	..	1 oz.	B.S.	B.S.	B.S.	B.S.	B.S.												
12	F.	50	F. A.	Stationary	..	..	..	..	..	B.S.	B.S.	B.S.	B.S.												
17	F.	35	F. A.	Slightly prog.	..	..	..	..	..	..	..	1/16 oz.	1 oz.	4 oz.[1]											
16	F.	24	M. A.	Stationary	..	..	..	..	..	..	..	..	..	..	B.S.	B.S.									
6	F.	27	F. A.	Stationary	..	..	..	..	..	..	..	..	..	..	..	B.S.									
99	F.	22	F. A.	Stationary	..	..	..	..	..	..	..	..	..	..	..	..	2 oz.	6 oz.	1/8 oz.						
4	M.	62	F. A.	Stationary	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	B.S.	..	..	B.S.		
81	F.	29	F. A.	Progressive	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	3 oz.	14 oz.	20 oz.[1]	
155	F.	35	M. A.	Stationary	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1/8 oz.	
166	F.	15	Inc.	Improved	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	B.S.

B. S. indicates blood-streaked sputum.
[1] Indicates immediately fatal hemorrhage (Nos. 116, 17, and 81).
[2] Patient died twenty-five days later, without recurrence of hemorrhage.

Even more remarkable are the number and severity of the hemorrhages in the female sex, all the six cases raising pure blood being females. The relative frequency of hemorrhages in males as compared to females has been variously estimated to be from a little less than 2 to 1 to a little over 3 to 1. Immediately fatal cases due to hemorrhage in females are considered to be very infrequent by Anders,[1] who was unable to find a single instance of fatal bleeding in 2453 female tuberculous cases, as compared to 10 fatal cases in 3420 males. Fatal hemorrhages at the Home for Consumptives have, as a rule, been of rather infrequent occurrence, only 1 case apart from the 3 here mentioned taking place within two years.

The immediately fatal cases were all far advanced, with extensive pulmonary lesions and cavity formation. No. 116 throughout her illness expectorated blood on nine occasions, exhibiting pure blood on six of these. No. 17 had a total of fourteen hemorrhages, of which thirteen consisted of pure blood. No. 81 had a total of thirteen hemorrhages, twelve of pure blood.

In one of the fatal cases the bleeding was associated with the menstrual period, half a dram of blood being expectorated on the day after the onset of the menses, one ounce on the following day, and on the next day the fatal hemorrhage occurring. It is by no means rare for hemorrhages to occur at the menstrual periods, in some cases recurring with a certain degree of regularity, and in fact the last hemorrhage this patient had been seized with ten months previously occurred synchronously with her menses. However, I have not met with a report of any other case in which a fatal hemorrhage took place at this time. Subsequently B. I. Macht[3] mentions a fatal case reported by Flesch.

The amount of the hemoptysis gives no definite indication of the quantity of blood lost or of the serious effects produced. This is well illustrated by the immediately fatal cases referred to in the table. Osler mentions a case in which the bleeding was fatal without the appearance of any hemoptysis, an eroded vessel having opened into a large cavity. The immediate effects of a hemorrhage will depend on the amount of blood lost, on the degree of suffocation, or on both.

How is the occurrence of hemorrhages in groups of cases to be explained? So many and so severe cases as this series presents can hardly have been the result of a mere coincidence, and one looks for some common cause or causes to explain the whole group.

Exertion, excitement, etc., may be excluded as causes in this outbreak, as all the patients were leading quiet lives, all the ones with fatal hemorrhages having been in bed for some time previously, and some of the severe hemorrhages having occurred at night. In fact, I can recall no case in which a hemorrhage at the Home could be traced to exertion, and many of them have taken place at night.

Seasonal and atmospheric conditions have been offered as causes of hemorrhages. On this supposition two explanations suggest themselves: (1) that these conditions affect the foci of disease, thereby producing hemorrhages; and (2) that they in some way affect pathogenic bacteria or render their hosts more susceptible, the resulting activity of the germs causing hemorrhages. Colds, bronchitis, pneumonia, and even the hemoptysis of phthisis have been stated to be more frequent in winter and spring than in summer and early fall.

West, however, finds in statistics no proof of any seasonal influence on the occurrence of hemoptysis. The present outbreak occurred at a time of year generally considered to be pretty healthful. In the year under consideration the rainfall and temperature were both below the average for this particular period.

Minor[4] states that "he has noticed that close, damp, hot spells, with a low barometer, seem to be the time when many cases of hemorrhages are apt to occur, and that this bunching is much less common in winter. Thus, in the practice of Dr. W. L. Dunn, in the summer of 1907, sixteen hemorrhages occurred among his patients in one week."

Of the various explanations offered to account for these hemorrhagic outbreaks, the most reasonable seems to be that some of them are due, at least in part, to an acutely infectious origin. Such a conclusion, however, is drawn much more from inference than from definite scientific data. An infectious origin is suggested (1) by the grouping of the cases; (2) by the evidences of toxemia, such as fever and pain; (3) by the development of definite acute infections in some of the cases of hemorrhage, for example an acute pneumonia; (4) by the occurrence at the same time in other patients of symptoms of acute infections like acute colds; and (5) by bacteriological examination of the sputum and lungs in a limited number of cases.

As to the first point, this series of cases is simply an exaggeration of what is constantly being encountered in institutions. Indeed, so frequently do hemorrhages occur in groups of cases that one is disposed to regard the appearance of one case as the probable herald of more to come.

A rise in temperature, both in those patients spitting pure blood and those with only streaky sputum, occurs sufficiently often to suggest an acute infection. However, such a rise is frequently absent, and among our 14 cases occurred in only three. This absence of fever is not surprising if one supposes that the causative agent consists in the microörganisms of acute intercurrent infections, like acute colds, which in normal persons may cause hardly any rise of temperature. Many tuberculous patients already have some fever, while advanced cases often show very little tendency to febrile reactions.

The records as to pain are too few in the present series to be of value, but pain is a frequent accompaniment of hemorrhage from the lungs. The pain is more apt to be localized to some spot or area of the chest than to be distributed over the body, thus differing from the general pain often encountered in the toxemias of acute infections in non-tuberculous individuals. West[5] has called attention to the pain preceding hemorrhage and relieved by it. He attributes the pain to a more or less sudden congestion. Wood[6] believes that evidences of pleuritis in phthisis may be due to a toxemia from infections of the upper respiratory tract, the pleura in many of these cases being a point of lessened resistance. It seems quite possible that toxemia may at times cause congestion, which in turn may produce both pain and hemorrhage. Localized tenderness of the chest is another frequent accompaniment of hemorrhage. I[7] have reported 8 cases of pain among 10 cases with hemorrhage, and 10 cases of tenderness among 11 cases with hemorrhages.

The theory of an infectious origin is further supported by the symptoms suggesting an acute bronchitis, such as increased cough and expectoration, tightness or a sense of oppression in the chest, and dyspnea. Patients are frequently forwarned of hemorrhage. and West records a patient who could always foretell the onset of a hemorrhage by the pain in the chest. Moreover, at the time of these outbreaks other patients may be suffering from acute colds, though not themselves spitting blood.

The frequent occurrence of small amounts of blood in acute infections of both the upper and lower respiratory tract even in the absence of tuberculosis is significant. McPhedran[8] states that the bacteria most often found in acute bronchitis, when not due to specific infections, like influenza, pertussis, typhoid etc., are the pneumococcus and streptococcus, which may occur singly, in association with each other or with other bacteria. Osler[9] mentions a case of hemorrhage in typhoid in which the lungs at autopsy revealed no lesion. Flick, Ravenel, and Irwin[10] have found in the sputum and lungs from hemorrhagic tuberculous cases a number of organisms, but attributed most importance to the pneumococcus, being impressed by the association of pneumococci and hemorrhages in cases of pneumonia.

It would be valuable to know whether acute intercurrent affections of the respiratory tract occur less at some localities than others, and whether there is a corresponding decrease in the number of hemorrhages. The more isolated the sanatoria the more infrequent one would expect to find these acute infections. At Fort Stanton, New Mexico, Smith[11] did not observe any grouping of the cases of hemorrhage (cases with only streaky sputum being excluded), nor any special association between hemorrhages and the humidity or barometric pressure.

Undoubted evidences of acute infection are at times encountered

even when the hemorrhage is large. Sudden high fever, consolidation in the lung, and death may occur within a few days or weeks after a hemorrhage. While in some of these cases infection follows insufflation of blood, in others the infection is primary, and the hemorrhage is a result.

Considerations like the preceding with all their deficiencies and inconsistencies lend weight to the idea that a certain number of hemorrhages may be due, at least in part, to prevalent, that is, contagious intercurrent affections, probably including the common colds. It is natural to suppose that the resulting congestion would particularly affect tissue already injured by disease.

While we often cannot differentiate by means of the symptoms and physical signs between renewed activity of the tuberculous process and some other process—for instance, some intercurrent affection—we may assume that in a certain number of cases only the latter has been in progress, when the symptoms and signs are slight and disappear in a short time without leaving any appreciable traces of their action. Thus blood-streaked sputum, and at times quite large hemorrhages, occur in apparently healed cases of tuberculosis, being accompanied by symptoms of an acute infection, which soon pass off, leaving the patient as well as before.*

Just what all the operative factors may be in the diseased focus at the time of a hemorrhage cannot be determined. In those cases in which we assume there is no renewed activity on the part of the tubercle bacillus or fresh output of tuberculous toxins, the focal phenomena cannot be specific in character, only the toxins of the tubercle bacillus and not those of other bacteria having any specific action on tubercular foci (Denys[12]). Perhaps there is sufficient congestion in some of the cases to excite hemorrhage in a focus already diseased, and containing bloodvessels with weakened walls, so that it apparently offers less resistance to even purely mechanical factors, such as increased blood pressure. In a similar way increased intravascular tension may be supposed to act upon a tuberculous area in cases of menstrual hemoptysis, the focus of disease, however, revealing no evidences of activity at the time of the menses.

On the other hand, if increased blood pressure at the focus of disease is the only exciting cause of these hemorrhages, why does not violent exertion more frequently cause them? With sudden exertion the rise in pressure comes on much more abruptly even if it is less sustained than in acute infections or during the menses. Therefore, in the latter conditions some factor or factors additional to the increased blood pressure would seem to be operative. The circulation in the blood during an acute infection or during menstruation of substances that have some effect on diseased tissue

* In the discussion Dr. Gwyn referred to a case of apparently healed tuberculosis that had a hemorrhage during an attack of mumps, no evil consequences following.

predisposing it to hemorrhage may possibly be a partial explanation, without, of course, having any data in its support.

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MOUNTAIN SICKNESS.

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Travelling and sojourning among mountains is a prominent feature of modern life, because of the increasing enthusiasm for Nature's grandeur and the growing appreciation of the hygienic factors of the climate of high altitudes by the healthy as well as by the sick. The number of resorts and sanatoria in the regions of high mountains is ever increasing, to combat various diseases, successfully, as the empiricism of centuries has proved.

But as the advances became bolder, penetrating into the highest altitudes, partly for touristic purposes, partly for scientific exploration and research, and as mountain wandering became more common, due to successful geographical exploration and development of railways, that added to the accessibility of the higher mountain systems, experiences accumulated, that pointed to harmful effects and dangers from the climate of high altitudes above a certain zone. The study of these effects, that high altitudes exert upon the human organism in a physiological and pathological sense, is highly interesting from a scientific point of view; it also has an important bearing upon the practical question. How may the hygienic factors of high lands be utilized to the best advantage by both the sick and the healthy, and what are the indications and contraindications for high altitudes?

The increasing numbers of Americans that resort to the European Alps and to the high elevations of the Rocky Mountains in our Western States make this subject one of concern to all physicians.

The Federal Government of Switzerland considered it of great practical importance to ascertain, when the construction of mountain railways to the highest summits of the European Alps was contemplated, where the danger line was, at what altitudes injuries to the health of visitors might presumably be inflicted, and which individuals might be seriously imperiled. In connection with these studies, Kronecker's account of his observations in the pneumatic chamber, and on mountains, is one of the most important works written on mountain sickness. But also reports were then available of experiences made on the high mountain railroads of the American continent, especially on the famous Oroya Railroad in the Peruvian Cordillera, the highest railroad of the earth, reaching the considerable elevation of 15,800 feet, and also of experiences on the cog-wheel railroad to the summit of Pike's Peak, 14,200 feet.

Historical Remarks. The exploration and conquest of the high European summits had not yet commenced when the Spaniards, on their conquering expeditions into the equinoxial regions of ancient American civilization, penetrated into the mountain chains of the Great Andes, and advanced to altitudes where they could not escape the serious effect of the rare climate upon the health. Numerous are the records of this period of conquest, vividly narrating the great agonies and miseries which the bold pioneers had to endure on the high passes of the great Andes.

Perhaps the most interesting are those of the Jesuit, Pater Acosta, who, as the first one in his *Historia naturale de las Indies*, gives us a detailed account of the symptom complex which he named mountain sickness.

On his expedition to Peru, at the altitude of about 14,800 feet, when passing the Periacaca on his mule, he was seized by an attack of discomfort, with abdominal cramps and the vomiting of food, mucus, and bile, and finally blood; his companions suffered from similar attacks, and also from diarrhea. It deserves to be mentioned that he ascribed these symptoms to the rarity of the atmosphere.

Neglecting a few records from the following period, we see their number rapidly grow at the end of the eighteenth century, the beginning of the period of great scientific explorations of the higher mountain systems of our earth, relative to their geography, orography, geology, etc.

De Saussure relates that, during his famous expedition on the summit of Mont Blanc in 1787, an overwhelming sleepiness, which defied cold, wind, and snow; lethargy, lassitude, vanishing of muscular power, and vomiting was experienced among the participants of the toilsome ascent. He had to take breath every

ten to fifteen steps, being compelled by exhaustion to sit down. When trying to rise up again his legs failed. The fatigue, which he explained by rarity of air, was overwhelming. He suffered from intense heart palpitation, beating of the arteries of the head, much dyspnea, a feeling of faintness, and complete loss of appetite.

In his records he at the same time points to the remarkably speedy recovery from the exhaustion after a short rest of two to three minutes, so differing from the symptoms of exhaustion in low altitudes due to actual overexertion.

On the summit of Mont Blanc, 15,800 feet, where he made meteorogical observations, he suffered at rest only from slight nausea, but every attempt at reading his recording instruments in the rarefied air was followed by intensive dyspnea as a consequence of the short suspension of respiration due to the intentness required for the observation.

In the beginning of the nineteenth century, Alexander von Humboldt[4] undertook his well-known scientific expeditions to Central and South America, where he explored the great mountain chain of the Cordillera, in its average height, the second on earth. Thrillingly he depicts the sufferings which befell him at the altitude of about 5800 meters (19,000 feet), during his ascent of the Chimborazo volcano, that, towering with its five summits, reaches the height of 6250 meters (20,600 feet).

"The Indians, with one exception, abandoned us at an altitude of 15,600 feet. Prayers and threats were alike vain; they declared they were suffering more than we. When the height of 5800 meters (19,000 feet) was reached, all of us by degrees began to feel very ill at ease and to suffer from great nausea; the vomiting was accompanied by dizziness, and was more distressing than the difficulty of breathing. The companions bled from gums and lips, and the conjunctivas of their eyes likewise were bloodshot."

Once when upon the Pinchincha, at an elevation of 13,800 feet, he was seized with such violent pain in the stomach and overpowering giddiness that he sank upon the ground in a state of insensibility.

Vivid pictures of self-experienced sufferings during travels among the great Andes we owe also to Poeppig, of Leipzig, Tschudi, Whymper, Conway, and others.

Tschudi,[13] who travelled in Peru from 1838 to 1842 (*Travels in the Great Andes,* translation from the German), depicts one of his attacks of mountain sickness at an altitude of about 4500 meters (14,800 feet) in the Cordillera.

"My panting mule slackened his pace and seemed unwilling to mount a rather steep ascent. To relieve him I dismounted and began walking at a rapid pace. But I soon felt the influence of the rarefied atmosphere, and I experienced an oppressive sensation, which I had never known before. I stood still for a few moments

to recover myself and then tried to advance; but an indescribable oppression overcame me. My heart throbbed audibly, my breathing was short and interrupted. A world's weight seemed to lie upon my chest; my lips swelled and burst; the capillary vessels of my eyelids gave way, and blood flowed from them. In a few moments my senses began to leave me. I could neither see, hear, nor feel distinctly. A gray mist floated before my eyes. In this half senseless state I lay stretched on the ground until I felt sufficiently recovered to remount my mule."

Dwelling upon the subject of mountain sickness, he mentions the fact, that high altitudes are very fatal to cats. At the elevation of 18,000 feet above the sea, these animals cannot live; numerous trials have been made to rear them in the villages of the upper mountains, but without effect, for they die soon here under convulsions. Horses and mules suffer like man.

It is only more lately that experiences as to mountain sickness in the great mountain systems of other geographical positions have been gathered, a fact which may be explained by the circumstance that the great Andes of Peru and Ecuador are only to a small extent covered with eternal snow and glaciers, on account of their equatorial latitude, and for that reason they have been inhabited from time immemorial to very considerable elevations, and, therefore, are comparatively easy of access.

The temperate climate renders it possible, as high as Quito, 2850 meters (9400 feet), for bananas, palms, and eucalyptus to grow on protected places, and an abundant flora of alpine flowers ascends to an elevation of 4000 to 4800 meters (13,000 to 15,800 feet).

Thus, numerous records have been made of observations on mountain sickness during various ascents of the summits of the Caucasus, the Ararat, 5200 meters (17,000 feet), of Mount Loa, 4170 meters (13,760 feet), etc., and finally during travels on the great Central-Asiatic high plateaus of Thibet, and in the Himalayas (Sven Hedin, Guillermod, Kronecker, and others).

The authors emphasize the fact that the higher the altitudes the greater is the difficulty of walking and breathing, and that physical exertion even of a minor degree augments the suffering in an extraordinary way.

The brothers Schlagintweit, well possessed of an extraordinary resistance against the air of high altitudes, who on their scientific mission to high Asia succeeded in carrying their climbing as high as 6800 meters (22,000 feet), corroborate the fact that the native Hindoo coolies, the carriers of burdens, are often more affected than the European travellers who are riding. "Our guides and servants," he states, "dropped upon the snow, declaring they would rather die than take one step more."

Whymper,[14] the well-known English high-tourist, who, among

mountain climbers, has devoted more particular attention to mountain sickness, experienced manifestations of mountain sickness, as related in his work on the Chimborazo in the region of 16,000 feet above the sea, corresponding to a barometric pressure of 400 mm. After a meal he and his two companions were suddenly seized with an alarming attack of the malady, with great weakness, fatigue, thirst, headache, a feeling of fever, extreme dyspnea, heart palpitation, and acceleration of the pulse. He adds this remark: "Our incapacity was neither due to exhaustion nor to deficiency of bodily strength, but to the rarity of air."

Definition and Symptoms During Work. Scrutinizing the accounts of pathological phenomena that occur during travels in high mountains, in order to define the clinical entity of the mountain sickness proper, we ought to regard only manifestations that in a direct or specific way are due to the high elevation itself, and we must subtract those that may come from causes also operative in lowlands, that is, symptoms of an actual overexertion, snow blindness, erythema solare, etc.

The mountain sickness befalls some individuals at a lower, others at a higher altitude, but no one who proceeds beyond a certain elevation, the critical line, escapes the malady. An elevation of 3000 meters (10,000 feet), or even less, might provoke it in some, others may escape the symptoms up to 4000 meters (13,000 feet), or even 5000 meters (16,500 feet), while only very few, possessed of unusual resisting power, can without much distress venture upward to 6000 or almost to 7000 meters (19,000 to 23,000 feet).

The symptoms of mountain sickness depend not only on the nature of the individual, but also on various intricate contingencies, especially on physical exertion, that is, on whether the ascent is performed by climbing or by passive carriage on horseback, sedan chair, or mountain railroad.

In the former case, as might be expected, the symptoms make their appearance in lower altitudes, and involve those organs which are under the greatest strain, namely, the heart and muscles. Marching or climbing within the critical zone causes fatigue, faintness, and physical prostration, that often set in rather suddenly and after even a comparatively small amount of physical work; they may be so severe as to necessitate rest, or even to lie down; the failure of the muscles to act may completely incapacitate the traveller for movement. But in not extreme elevations, a few moments of repose apparently restore the former strength, and with new muscular vigor one takes up again his climbing, to be forced, however, to halt anew after perhaps only a few steps.

The great intensity of the fatigue, the readiness with which it appears upon even moderate muscular activity, which in low altitudes hardly would have any perceptible effect, distinguish it strikingly from ordinary fatigue, called forth by actual overexertion.

The strange feeling of faintness and the quick exhaustibility in mountain sickness, therefore, is not identical with ordinary exhaustion by excessive muscular work, but it is generally admitted to be due to the deficiency of oxygen in the rarified air, that cannot satisfy the body's increased demand on account of the increased work of the heart and muscles.

But speedy reparation takes place for when at rest, the consumption of oxygen falls off rapidly.

To the above-mentioned fatigue and weakness are added heart palpitation, dyspnea, oppression of the chest, vertigo, anorexia, headache, often ringing in the ears and impairment of hearing, nausea, vomiting, great drowsiness, and sometimes syncopal attacks.

That cases of genuine overexertion with the well-known trail of serious symptoms, such as acute dilatation and insufficiency of the heart, feeble dicrotic "fatigue" pulse, etc., are encountered in mountains more frequently than in lowlands is not to be wondered at, as mountaineering represents intense muscular work, often carried beyond the limits of endurance and capacity for muscular exertion, in the case of untrained summer tourists, either from necessity or temptation.

But these symptoms are not from mountain sickness primarily, being similar to those occurring in overexertion in lowlands; though more grave significance is attached to them on account of the rarity of oxygen in higher altitudes. Recovery takes place more slowly and exitus lethalis is more liable to be the issue.

In pronounced cases of mountain sickness, as, for instance, in very high altitudes, psychical manifestations may supervene. The will power is then extinguished, mental lassitude prevails, and in consequence a complete indifference toward the dangers of snow, cold, storm, etc., gets hold of the individual, "who would rather die on the spot than make an attempt to proceed."

States of mental excitability, as well as states of physical depression, are encountered; increased liability of the emotions tending to quarrelsomeness or hilarious expansivity. This is well known to the guides and tourists of the Alps. Cyanosis, blue circles around the eyes, bleeding from nose, lips, gums, lungs, and stomach, and constipation or diarrhea, are other symptoms referred to in the records on mountain sickness.

Author's Experience. I experienced the effect which comparatively moderate altitudes exert, in tending to lower physical endurance, on the high plateau of the Yellowstone geysers, the elevation of which is about 7000 feet, where fast marching or, more markedly, running on a horizontal level for a short distance such as 300 to 350 yards, called forth a very high pulse rate (150 to 160) and dyspnea, that I never experienced at lower levels with such insignificant muscular work. Many tourists, although trained in various sports,

expressed their wonderment at how quickly fatigue arose when they wandered on the fairly horizontal plateau of the geysers.

When I had reached the critical line, in ascending the volcano Etna (10,800 feet), at an altitude of about 9600 feet, the rarefied atmosphere made itself felt to me in a considerable degree; in spite of a good night's rest in the observatory at the base of the central cinder cone (9650 feet), the final stage of the ascent was made under great fatigue, heart palpitation, very high pulse rate and difficulty of breathing, so that I was forced to halt every fifteen to twenty-five steps, but restoration of apparently full muscular strength promptly occurred after a rest of only one to two minutes. It was obvious that exhaustion due to actual overexertion was out of the question, for the smooth cinder sides of the cone, inclined at a slope of about 30 degrees, were rather compact on account of previous rains, so offering a splendid foothold. On the top, at rest, I felt perfectly well.

Perhaps tourists here show manifest symptoms of mountain sickness, such as lassitude, headache, apathy, nausea, vomiting and dyspnea at the slightest movement, etc., more frequently than on other mountains of the same altitude. This is possibly due to the fact that the ascent begins practically at sea level, and is performed without intermediary stages.

Symptoms of Mountain Sickness Without the Influence of Exertion. As the influence of the muscular exertion of climbing, or of occasional actual overexertion, renders the clinical picture more complex, and, therefore, rather difficult of analysis, we may study with great advantage the syndrome that arises when a high altitude is reached passively, that is, without physical work, as by mountain railroad, riding on horseback, or by ascending in a balloon. Here symptoms are forthcoming that at first point to disturbances of the brain functions; such as headache, dizziness, trembling, apathy, lassitude, and sleepiness, to which are added general weakness, often tinnitus aurium, nausea, and vomiting, sometimes obscuration of the vision and, if aggravated, even syncope.

Moderate exertion, as wandering on a level, or to a greater degree climbing, increases the manifestations, or if they have not been developed, calls them forth; dyspnea sets in, and the pulse quickly rises to a very high rate. The disturbances during high balloon ascensions are similar. However, the symptoms mentioned, as a rule, do not appear immediately after the arrival on the height, but may develop gradually, that is, within hours, the speed of the passive ascent having an important bearing. Complete loss of appetite also prevails; thus, the whole picture resembles the state of acute anemia.

Author's Experience on Pike's Peak. In 1908 I made an ascent of Pike's Peak (14,200 feet) by the cog-wheel railroad. The trip to the summit took one and one-half hours. After arriving, about noon, my pulse rate at rest was increased to 70, the respirations

to 30. Attacks of dizziness, sensations in the ear, tremor of the hands, and a desire of more frequent and deeper respiration, often with sighing, were the clinical manifestations. Moreover, dyspnea and dizziness became aggravated and the pulse rate very much increased by ridiculously insignificant exertions, as by leaping over the granite blocks on the summit, by fast walking, and especially by stooping; I was unable to tie my shoes without pausing in between to gasp for air; and oftentimes I had pulsations in the eyes. I passed in bed an entirely sleepless and miserable night, on account of malaise and attacks of slight oppression of the chest. The pulse rate was between 90 and 100, the higher rates after slight movements. Most of the night there was a pronounced periodical type of breathing, approaching Cheyne-Stokes' phenomenon, namely, long pauses, during which my drowsiness increased, were followed by a series of a few very deep inspirations, which in their succession gradually became superficial ones.

The following day the attacks of dizziness and the pulsations in the bulbus had improved.

The lowest altitude in Colorado at which I experienced dizziness, that at the same time caused uncertainty in walking, was at 10,800 feet, when going over Marshall Pass by railroad.

Under physiological conditions in low land indications of a periodical respiration can only be observed, during sleep, when the depth of the respiratory movements, gradually increasing and decreasing, forms thus connected groups.

This physiological phenomenon is explained by the assumption of a lowered irritability of the nervous respiratory centre during sleep. In high altitudes, however, this periodicity is more pronounced, and the respiratory curves are also undulating while awake. Mosso observed it on the summit of Monte Rosa (15,300 feet) in almost everybody.

The types of the respiratory periodicity in high elevations are various, as illustrated in Mosso's monograph,[9] and include also characteristic Cheyne-Stokes' phenomenon. The occurrence of the latter in very high altitudes, however, has not the ominous significance that otherwise is attached to it.

Prognosis. Although the malady may have aggravated manifestations with great discomfort and distress, in moderate altitudes these, with time, especially when at rest, tend to diminish rather than to increase, and the danger to those otherwise healthy, is generally slight. However, a few cases of exitus lethalis are ascribed to the direct effect of the rarefied atmosphere; the French scientists Sivel and Crocé-Spinelli, lost their lives in their balloon at an altitude of about 8600 meters, while Tissandier, the third participant of the ascension, fell unconscious and narrowly escaped.

Accommodation and Acclimatization. As a rule, in the course of days or weeks, a certain degree of acclimatization takes place.

The laborers occupied with the boring of the Mont Blanc tunnel suffered only in the first weeks from short breathing, drowsiness, loss of appetite, and great exhaustibility.

There are many permanently inhabited places on the slopes and high plateaus of the Andes up to the considerable elevations of 13,000 to 15,000 feet; and the mines here of Villacota, situated at an altitude of 5000 meters (16,500 feet) are operated by indigenous and foreign laborers. The natives of the places are capable of speedy marching in heights where newcomers from Lima suffer great distress.

In Quito, 2850 meters (9400 feet), a city of 50,000 inhabitants, bull-fights are performed, and in Potosi, 4000 meters (13,200 feet), "the girls can dance throughout the night as in our country."

However, it must be mentioned that the adaptibility of the human organism is limited, the acclimatization being effective only in those altitudes in which one stays permanently, while failing completely in extreme heights as at 6000 meters (19,800 feet).

Causes. The physiological and pathological manifestations observed in high altitudes, as described, can experimentally be produced by gradually rarefying the atmosphere within a pneumatic chamber, imitating thus the decrease of the barometric pressure and of the amount of oxygen with the increasing altitude. Such experiments, "artificial ascents," under various conditions, have been made by Paul Bert,[2] Mosso,[8] Reynard, Schroetter, Zuntz, Löwy, and others on men and animals, as on monkeys, cats, dogs, guinea-pigs, birds, etc., to elucidate the etiology and pathogenesis of mountain sickness.

As the air in the chamber gets decompressed, the individual in lying posture first notices, perhaps, a slight feeling of pressure of the head, buzzing in the ears, and an increasing tiredness and drowsiness, which with the proceeding diminution of the air, more and more becomes irresistible. Slight exertion, for instance, sitting up, handling apparatus, or stooping, aggravates the fatigue and faintness considerably, the muscular strength fails, dizziness and ataxia occur, the eyesight is dimmed, the psychical functions—for instance, the memory, attentiveness, concentration, etc.—are impaired, and headache, dyspnea, heart palpitation, sometimes also nausea, manifest themselves. After lying down again, or by inhalation of oxygen, the symptoms improve or may disappear entirely.

Animals get less lively, motionless, often vomit, and fall into a doze or unconsciousness.

The muscular ataxia in much rarefied air shows itself also in alterations of the handwriting. Of this, H. v. Schroetter, at an air pressure of 240 mm., after a short interruption of oxygen inhalation, has given a striking example; his hand became hardly legible.

Zuntz[17] reports the observation of similar alterations of the hand-

writing of Caspari and Mueller on the summit of Monte Rosa, 4650 meters (15,300 feet), and, according to him, very marked is the loss of control of the voluntary muscles shown in the meteorological notes of Berson and Suering[1] during their well-known balloon ascent in 1901, whereby they reached the highest altitude as yet obtained by man—10,800 meters (35,600 feet).

The theory at the present time accepted by most investigators as to the causation of the malady in high altitudes holds the rarity of the oxygen in the atmosphere responsible. It causes a diminution of oxygen in the blood, a state of "anoxhemia barometriea," as Jourdanet, the founder of this theory, has termed it, and consequently a kind of asphyxia of the tissues.

Inhalations of oxygen in the pneumatic chamber and in the balloon have a beneficial effect, retarding or relieving the symptoms, and rendering man capable of withstanding degress of air rarity or altitudes which otherwise would be fatal.

During high ascensions, after the first draughts of oxygen the strength of aëronauts returns, fainting fits disappear, the beginning psychic lethargy changes to clear consciousness, physical work can be done again, etc.

With oxygen inspiration, Paul Bert[2] could submit himself in a metal cylinder to a decompression of the atmosphere which corresponded to altitudes of the summit of Chimborazo and of Mount Everet, the highest mountain on earth.

Mosso, in his experiments, endured thus an air pressure corresponding to an altitude of 10,500 meters (34,600 feet), and Suering in his balloon ascension could with oxygen supply make the record of an elevation of 35,600 feet, the highest as yet obtained.

In connection with such facts arises the question, interesting from a physiological and biological standpoint, as to the maximum altitude compatible with human life.

H. v. Schroetter[12] (Vienna), by calculation, places the limit at about 12,000 meters (39,000 feet), for here even inhalation of pure oxygen would be without avail, because at such an altitude the partial pressure of oxygen in the lung alveoles would be too low to allow its absorption.

The great exhaustibility by muscular work in high mountains has its analogy also in the experiments of Reynard, 1894, who found that a guinea-pig, forced to move about within the recipient of an air pump, at an air pressure corresponding to 4600 meters (15,000 feet) altitude, very soon became exhausted and fell, while another guinea-pig, left at rest, fell and seemed to die only at an air pressure which corresponded to an altitude of 8000 meters (26,400 feet). When air was quickly admitted, both animals recovered, the first one, however, very slowly.

Anoxyhemia gives a satisfactory explanation for the fact that mountain sickness appears sooner during muscular work than at

rest, as during ordinary mountain climbing the demand for oxygen is increased four to five times more than the amount demanded during rest. Therefore altitudes such as have been reached in balloons can hardly be obtained by climbing, and the climbing up to almost 7000 meters (23,000 feet) in the Andes and Himalayas, as done by Conway,[3] Zurbrigger, and Stuart Vines, although with difficulties, must be considered as an extraordinary feat and as a proof of a very rare resistive power.

The accumulation of pathological products of metabolism, that gradually develop on account of the insufficient oxygen supply in the blood and betray themselves not only in the increased output of incompletely oxidized substances in the urine, but also by the decrease of the alkalinity of the blood (Zuntz), may account for the fact that the effects of high altitudes often are cumulative, the manifestations often appearing not immediately upon arrival on the summit, but gradually within hours, or even posthumous, so to speak, during the descent.

The acclimatization to high altitudes is principally due to an increase in the total amount of hemoglobin as the oxygen carrier, and to an alteration of the respiration and circulation, in a regulative sense.

As a matter of fact, the natives of the high plateaus of the Andes show a remarkably higher number of erythrocytes than the inhabitants of lowlands, namely, 6,000,000 to 8,000,000 in 1 c.mm.; a gradual increase of the number of red blood cells is also observed in man and animals, who temporarily remain in high altitudes.

Paul Bert, in 1882, found that the blood of the Peruvian mountain sheep (llama) was capable of absorbing much more oxygen than was the blood of sheep living on the plains.

Miescher[7] suggested, and Zuntz and Löwy proved by experiments on animals, that the air of high elevations stimulates the function of the red bone marrow; the total amount of blood and hemoglobin which could be extracted from the body being acually increased.

Jaquet[6] obtained quite similar results by keepting rabbits in chambers in which the atmospheric pressure was artificially reduced.

Humboldt found a remarkable increase in the capacity of the thorax among the inhabitants of the great Andes, and Dr. C. T. Williams[15] likewise observed an actual increase in the thorax as the result of a residence in high mountain resorts.

Besides the diminution of oxygen in high mountains, some accessory factors, the sum total of the other climatic factors, including the minute electric conditions of the atmosphere, seem to have a certain bearing upon the outbreak of the malady, although not yet well understood. Intensive cold temperatures, dry air, clear skies, when, as it is found, the ionization of the atmosphere is increased, and also strong sunshine are, according to the general experience, largely contributory to the provocation or aggravation

of the symptoms, while vaporous air, cloudy skies, and winds tend to retard or lessen them. A very frequent statement is made that during the night's repose the symptoms become more distressing. Likewise very remarkable is the fact that the symptoms of mountain sickness may appear especially on certain locations of predilection, as is well known on the Alps and the Andes, though other regions of the same mountain range, or of the same mountain even situated higher, may allow mountaineering without suffering. Such places of predilection often are narrow couloirs, ravines, trough-shaped depressions of the niveau, in short, locations more or less protected from the motions of the air, and, therefore, not ventilated. On such places, according to Elster, Geitel, and Zunts, a high ionization, unipolarity, and radio-activity of the air exist as the result of the stagnation of the radio-active emanations from the soil. Saake[10] found the air of high altitudes to possess three times the amount of radio-active emanations than the air of lowlands, and it is known that certain soils and minerals, for instance, those containing pitchblende or some other metal ores, some clays, etc., emit a greater amount of emanations than others. But further investigation and advance of our knowledge of the influences which the minute electrical and other physical conditions of the atmosphere exert upon the human body, as yet hypothetical, will be necessary before we can pass on the problems that the above-mentioned facts involve. Obscurity prevails also in regard to an explanation of the circumstance that in the different mountain systems of our globe this sickness begins at different altitudes; in the European Alps, for instance, at about 3000 meters (9900 feet) many men suffer, while in the Andes the critical zone is located at about 4000 meters (13,000 feet), and in the Himalayas at about 5000 meters (16,500 feet).

Although the hypothesis that anoxyhemia is the cardinal cause of mountain sickness is at the present time accepted by many authorities, still because there seem to be difficulties in applying this theory to some phenomena, other authors have attempted explanations starting from different points of view.

Kronecker,[5] for instance, assumed that the diminution of the air pressure calls forth a hyperemia and blood stasis of the lungs, which is followed by an affection of the cardiac function and circulation; however, this mechanicophysical hypothesis has no foundation in the findings made by other authors.

Mosso,[8] who, in the Regina Margherita hut on the summit of Monte Rosa, made numerous observations and experiments, gathered experiences that led him to the conviction that the deficiency of CO_2 in the blood, the aknapia, as he names this condition, in contradistinction to asphyxia, was the agent provoking mountain sickness and not the lack of oxygen, the asphyxia of the tissues.

Zuntz,[17] Löwy, Mueller, and Caspari, in their recent work on

the climate of high altitudes, are quite opposed to Mosso's ingenious theory, and the greater weight of evidence substantiates the theory of the anoxyhemia of Jourdanet and Bert.

As it gives the key to a better understanding of the processes of acclimatization, so it likewise enables us to comprehend the differences of the resistance power of the different individuals. In the first place, this depends upon the varying amount of hemoglobin, the oxygen carrier, and upon the form of respiration of the individual. Exact observations and systematic experiments made by Löwy, Zuntz, and others established the fact that deep respirations greatly increase the partial pressure of the oxygen within the lung alveoli, even with unchanged oxygen tension of the outer inspiration air, thus increasing the supply of the blood; simultaneously the mechanical acceleration of the circulation by stronger respiratory movements assures a better oxygen supply of the various tissues.

Therefore, in high altitudes, persons with a type of deep respirations are at a great advantage over persons of flat breathing; this type of respiration being essentially prophylactic against the acute affections of the human organism by a greater decrease of the barometric pressure. On the other hand, a weak nervous system, lack of sleep, disturbances of the functions of the alimentary canal by overeating, alcoholism, etc., increase the liability of the malady and aggravate its character.

Contraindications. Higher altitudes ought to be avoided by persons whose adaptability, on account of certain organic diseases, is below par; for instance, general weakness, or grave degrees of anemia and emphysema pulmonum.

High elevations, even such of 3500 feet, should be considered dangerous, especially for persons suffering from weak heart action, valvular disease, particularly mitral insufficiency and myocarditis, and such pathological changes of the bloodvessels as are found in arteriosclerosis, aneurysma, and nephritis chronica, with high blood pressure.

Most emphatically, in doubtful cases, muscular exercise must be cautioned against until the heart has, to some extent, adapted itself to the changed conditions.

Zangger[16] directs special attention to the dangers of rapid ascent by high mountain railways for elderly persons suffering from nephritis or arteriosclerosis, since syncope, angina pectoris, asthma cardiacum, and apoplexy are possible occurrences also on the return to the lowlands from these excursions.

Prophylaxis and Therapy. In summing up the experiences and the theoretical points, we must accord great prophylactic and therapeutic importance to a sufficiency of the oxygen supply to the organs.

Wherever feasible, some means of transportation (horse, mule, railroad, sedan chair, etc.), should be preferred to exhaustive active

climbing, although the speed of ascent by mountain railroads might for many persons involve an objectionable feature.

Good training of the muscles, heart, and respiratory organs in moderate elevations previous to climbing to higher altitudes is paramount to increasing the resistance power; mounting should be done gradually and leisurely by small stages, so that there may be no abrupt transition, and the climber should be in good physical condition, avoiding extreme fatigue and exertion, which, like sleeplessness, increase the disposition to mountain sickness. The respiration should be deep, the nourishment sufficient and suitable, avoiding digestive disturbances, which by meteorism are apt to interfere with deep respiration.

When travelling by railroads that cross high altitudes, oxygen should be at the disposition of the persons suffering from manifestations, or, as Melinovski, chief engineer of the Oroya Mountain railroad, suggested, cars hermetically closed should be attached to the train, in which a suitable air pressure could be maintained artificially.

When the mountain sickness has set in, absolute rest, deep breathing, or oxygen inhalation will bring temporary relief, otherwise, with more serious symptoms, descent into lower altitudes must be resorted to before a new ascent can be considered.

Against the headache, antipyrine, phenacetine, etc., may be tried.

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REVIEWS

Modern Treatment: The Management of Disease with Medicinal and Non-medicinal Remedies. By American and English Authorities. Edited by Hobart Amory Hare, M.D., Professor of Therapeutics and Materia Medica, Jefferson Medical College, Philadelphia; Physician to the Jefferson College Hospital. Vol. I; pp. 930; 105 engravings, and 31 full-page plates. Philadelphia and New York: Lea & Febiger, 1910.

The notable advance which the past twenty years has brought about in our knowledge of the etiology and management of disease has worked radical alterations in therapeutic procedures. Much, however, of this recent knowledge has been disseminated in a form unavailable for ready application by the practising physician. Therefore, a work such as the one under consideration has become a necessity, and its timely appearance must be regarded with decided satisfaction.

The first part of Vol. I deals with general considerations of drug therapy, and embraces chapters on pharmacology, prescription writing, and the toxic effects of drugs. In the opening chapter, H. C. Wood, Jr., discusses the relationship of modern pharmacology to practical therapeutics. Although he emphasizes the value of pharmacology in medicine, he unfailingly recognizes the limitations of drug therapy. In his excellent summary of the physiological action of drugs, he wisely groups drugs according to their clinical uses rather than into a pharmacological classification.

The chapter on prescription writing, contributed by Hunsberger, is worthy of comment. Written by a skilled practical pharmacist, it is replete with helpful suggestions. Many of the perplexing technical details that frequently confront the physician in his efforts to combine drugs to the best advantage are here explained.

The second part of this volume considers non-medicinal measures for combating disease. It is the largest division of the book, and properly so; embracing nearly four hundred pages, it stands in striking contrast to the hundred odd pages previously devoted to drug therapy. It is impossible, in a review of this length, to take up separately the various important subjects discussed in each chapter. Suffice it to say that in every instance the contributor is one whose ripe personal experience and broad knowledge is such

as to enable him to write with authority upon his particular phase of the subject. The result is a series of admirable essays.

Baruch and Shrady introduce their discussion of hydrotherapy by a timely warning to the medical profession to abandon polypharmacy for the more rational physiological remedies. A consideration of the physiological action of heat and cold precedes their detailed account of the numerous hydrotherapeutic methods and their therapeutic application.

Price has added materially to the value of his article on electrotherapeutics by explaining the physics and physiology of the varieties of electricity, before turning to their diagnostic and therapeutic uses. The careful reading of such a chapter as this would do much to dispel from the minds of many physicians erroneous conceptions, born of insufficient knowledge, of the uses and limitations of electricity in medicine.

The question of nutrition and food has been accorded proper prominence. The subject is well covered by Friedenwald and Ruhräh. After a consideration of the physiology of nutrition and the composition and values of the various classes of foods, they devote several pages to the question of rectal feeding. Infant feeding is taken up in a general way, no effort being made to enter into much detail. On the same broad lines they discuss the dietetic management of fevers, paying special attention to those acute infections in which feeding is of prime importance or of unusual difficulty. Finally, they outline the principles of dietetics involved in various visceral and metabolic diseases, entering more into detail when considering diet in diseases of the gastro-intestinal tract and in diabetes.

Chief interest naturally centres about the chapters on serum therapy and vaccine therapy, since they deal with the most recent evidences of therapeutic progress, and because the results so far obtained in these fields hold out the promise of far greater successes in the future. In these chapters abstruse and confusing subjects are explained in a manner so simple and direct that the reader cannot fail to be enlightened.

Park in his contribution on serum therapy devotes most of his attention to the employment of this form of treatment in diphtheria and tetanus. The use of sera in dysentery, typhoid fever, and cholera, as well as in other acute infections, is, however, given due attention.

The question of opsonins and the opsonic index is taken up by Potter and Avery before they discuss vaccine therapy. Although they admit that the method has been more or less abandoned by many workers, they feel that the last word has not yet been said concerning the true value of the opsonic index. They regard antityphoid vaccination as a procedure of undoubted advantage, and look with decided favor upon the intelligent use of vaccines in the pyococcic infections.

In the comparatively short chapter on glandular therapy, Beebe sets forth the true status of this form of treatment. He divests the subject of all exaggerated claims, at the same time making it evident that the organotherapy of today is based upon the firm foundation of scientific fact.

The last section of the book is devoted to a series of admirable chapters upon the treatment of the most important infectious diseases. The articles in this group, which particularly arrested the attention of the reviewer, were Riesman's chapter on the treatment of typhoid fever, that by Meara on pneumonia and pleurisy, and Landis' consideration of tuberculosis. This last mentioned chapter embodies much sound common sense, and many practical suggestions that cannot fail to be of value to all who are called upon to supervise the management of tuberculosis.

Taken as a whole, Vol. I of this work on treatment is noticeably well balanced, no undue prominence being given any one subject to the exclusion of others. The liberal yet judicious use of illustrations adds decidedly to the clearness of the text in many places. The scarcity of typographical errors is noteworthy in the first edition of a book of this size.

By reason of the wide range of subjects that it covers, and the thoroughly modern, scientific, and, at the same time, practical manner in which these are set forth, it is evident that the volume is destined to assume a leading position among English treatises on therapeutics, and richly merits the unqualified support of the medical profession. G. M. P.

Dislocations and Joint Fractures, By Frederic J. Cotton, A.M., M.D., First Assistant Surgeon to the Boston City Hospital, Assistant Professor of Clinical Surgery in Tufts College Medical School, Boston. Pp. 654, with 1201 illustrations, 830 from drawings by the Author. Philadelphia and London: W. B. Saunders Company, 1910.

There is an immense, indeed an amazing amount of work in this volume, showing that the author has cogitated and digested, argued and proved (or disproved), the matter of which it is composed many a time and oft during the five years or more which have elapsed while the book was making. It is a book entirely unlike most others, and herein consist its merits and its faults. Dr. Cotton says he has made an attempt to throw overboard all hereditary surgical views, to state what is really *known* of the subject today—to make a fresh start, so to speak, in this very important branch of surgery. He states with *naïveté*, "Wisdom did not begin with this generation, but we have had an unusual opportunity to learn,"

largely from the use of the *x*-rays and more frequent operative intervention. He boasts entire and sole responsibility for the contents of the volume; no one else has in any way assisted in its preparation, either as regards text or illustrations; the "first draft" of the work burst fully grown and clothed from his brain, like Minerva from the head of Jupiter; and references to "literature" collected later, were used mostly "for verification of fact and perspective, not for incorporation in the text." He acknowledges that perhaps this is not the right way to work, but excuses it as a reaction from the "benumbing German scholasticism," in which he was trained.

After an Introduction and a chapter on "Generalities," he discusses regionally the dislocations and joint fractures of the various parts of the skeleton, including jaw, spine, thorax, upper extremity, pelvis, and lower extremity.

He has a proper appreciation of the futility of expecting absolutely accurate apposition in fractures of the shafts of long bones, and of the misleading impression given to courts and laity by *x*-rays of end results. Yet he justly insists on exact reduction in fractures near joints, as restoring the contour necessary for useful function, and lessening the amount of callus formed. His views as to earlier (not necessarily *early*) motion of joints, so long as pain is not produced, will be commended by all modern surgeons; but his reference to the "frenzied lead" of some French surgeons (pp. 38, 39) perhaps indicates an imperfect comprehension of what really are the teachings of Lucas-Championnière and his followers. He claims that operation in recent fractures is now too indiscriminate, and he suggests, without expressing it, what is, no doubt, an absolute truth, that surgeons who are most insistent advocates of this treatment are those who are unable to secure by non-operative means as good results as their more conservative colleagues.

Dislocations of the shoulder, he holds, usually are produced not over the acromion as a fulcrum, but by the action of the tense adductor muscles with the arm in extreme abduction. His condemnation of the Velpeau bandage (p. 168) may depend on his ignorance of its proper application; certainly the curious arrangement shown in Fig. 119 is not a Velpeau bandage. He persists, like a few other surgeons, in calling an angular splint applied to the flexor surfaces of the arm and forearm an "internal" angular splint; whereas in exact parlance this term should refer to the Physick splint, and such a splint as Hartshorne's is more accurately designated an "anterior" angular splint.

In discussing lesions of the elbow Dr. Cotton is somewhat contradictory in stating (p. 212) that children are apt to fall on the elbow itself, not on the outstretched hand, thus explaining the less serious injuries encountered in childhood; while at p. 243 he states that the severe injuries met with in adults are to be explained on the score of direct violence, adults falling on the elbow, or having

it crushed in machinery, etc. It is also categorically stated (p. 273) that "separation of the *whole* lower epiphysis is possible up to four years of age," while Fig. 355, of a "boy of twelve years" is described as a "separation of the whole lower epiphysis of the humerus." In two foot-notes he attacks Dr. Warbasse for ignorance; and yet on the latter page exhibits his own by the bold assertion that in fractures of the external condyle "lateral mobility of the forearm as a whole does *not* occur;" and at p. 290 by his denial that physiological *cubitus valgus* owes its existence in part to a normal obliquity in the joint surface of the bones of the forearm at the elbow as well as in that of the humerus. In the treatment of supracondylar fractures at the elbow he is partial to a right angled moulded tin splint; but it can scarcely be doubted that if he reduced these fractures completely and put them up in hyperflexion (not merely acute flexion, as shown in Fig. 393), his results would be better, especially as regards the occurrence of *cubitus varus*, than those he has recorded elsewhere.

The merits of the book are many; its faults are not a few. It is suggestive, but it will serve no useful teaching purpose unless revised. It is weak in pathogenesis. There is endless tabulation of varieties and subvarieties of lesions, but there is no real classification. Rare lesions are often seen through a magnifying glass, but the myopia is too great to allow a vision in perspective. The illustrations are excellent (save a few which appear as if seen through a *camera obscura*, and a fewer still which look like nightmares), but they would have been still more excellent if drawn or even retouched by a real artist. The references to "literature" are fairly numerous, but valuable contributions (*e. g.*, Quénu and Küss on luxations of the metatarsals, the type of elbow fracture associated with the name of Prof. Posadas, etc.) would not have been overlooked if the author had had less contempt for scholasticism; and if he had enlisted friendly advice and criticism in the preparation of the text, so many contradictions and inconsequences would not have passed unobserved.

The work is in no sense a text-book. Its perusal, were such a thing possible for an undergraduate student, would give him such a confused and kaleidoscopic idea of dislocations and joint fractures as to unsettle his surgical reason forever. For those who have already learned a certain amount of perspective, and who can catch glimpses of the distant landscape through mists of beclouding detail, the volume is a storehouse of information, ideas, helps, suggestions, and inspirations to revise, correct, and improve their own practice.

A. P. C. A.

Operative Surgery. By John J. McGrath, Professor of Operative Surgery at the New York Post-Graduate Medical School. Third Revised edition; pp. 653; 276 illustrations, including many full-page plates in color and half-tone. Philadelphia: F. A. Davis Company.

It is stated in the preface of this book that particular care has been given to the section on abdominal surgery, and as a review of previous editions has been published, it may be well to discuss this section alone. The anatomy of the walls of the abdomen is well described, and the various methods for its incision are recounted. In the description of the operation, one might point out: That it is not necessary to pocket the subaponeurotic space in performing the Mayo operation for umbilical hernia; that Moynihan's method for total gastrectomy is somewhat better than the one described; that enterostomy for typhoid perforation as prescribed by Hays is omitted; that no mention is made of the "step" commonly practised in performing posterior gastrojejunostomy, whereby the edges of the transverse mesocolon are fastened either to the stomach or to the line of suture; that it is totally unnecessary and dangerous to dilate the stump of the appendix in order to invert it.

There is no mention of any of the operations for tumors of the bladder nor of the osteoplastic flap method in performing laminectomy. Silk or even silkworm gut is advised for suturing in the repair of hernia.

It is difficult to criticise a book of this character, because it consists, practically, of a compilation of established methods of surgical technique, but it does seem as though in a future edition the author should bring many of the operations more strictly "up to date." The greater part is excellent, and the volume of a handy size, well printed, and having comparatively few but generally adequate illustrations. G. P. M.

Bismuth Paste in Chronic Suppurations. By Emil G. Beck, Surgeon to the North Chicago Hospital, Chicago, Illinois. Pp. 237; 81 engravings, 9 diagrammatic illustrations, and a colored plate. St. Louis: C. V. Mosby Co., 1910.

Since Beck, in 1906, introduced the use of bismuth paste in the treatment of chronic suppuration there has appeared a great deal of literature upon the subject. This book, by the originator of the method, is especially timely as expressing the collective experience of the one most qualified to write on the subject. The contents include the use of the paste in diagnosis, in the treatment of sinuses and fistulæ, its limitation and the causes of failure, bismuth poisoning and its prevention, and its use in nose and ear work and

in dentistry. The text is lucid and exceedingly interesting—almost wonderful—the illustrations particularly good, and the size of the volume shows excellent judgment, there being no padding whatever. The method has made easy the treatment of conditions heretofore the bane of surgical practice, and nowhere can a clearer understanding of the subject be attained than in this book.

G. P. M.

Die Wassermannsche Reaktion mit Besondere Berücksichtigung ihrer Klinischen Verwertbarkeit. Von Privat-Dozent Dr. Harold Boas, I Assistenten am Rudolf Berghs-Hospital für venerische Krankheiten in Kopenhagen, mit einen Vorwort von Gen. Rat. Prof. Dr. A. Wassermann. Berlin: S. Karger, 1911.

This book of something over 180 pages is founded principally upon the personal observations of the author, who has had a very large and interesting experience with the Wassermann reaction. His conclusions, therefore, bear the mark of individual work, and are for this reason of special value. The entire subject is discussed in full and with a wide knowledge of the literature, a task which today has become most difficult, since the bibliography is truly appalling, covering in this treatise 44 closely written pages.

After an historical introduction, the technique is discussed in the second chapter. It is to be noted here that the Noguchi method is most inadequately described. Chapters follow upon control cases and the Wassermann reaction in the various stages and types of syphilis, and upon the influence of antisyphilitic treatment upon the reaction. Finally the question as to the meaning of a positive Wassermann reaction is discussed, and in this chapter the author upholds the view that a positive reaction indicates active syphilis.

W. T. L.

Difficult Labor. A Guide to its Management. By G. Ernest Herman, M.B., F.R.C.P., Consulting Obstetric Physician to the London Hospital. Fifth edition; pp. 547; 180 illustrations. New York: William Wood & Co., 1910.

As this book has now reached its fifth edition, any review in the true meaning of the term would be superfluous, and the duty of the reviewer is simply to call attention to the more important changes and additions contained in the book of 1910, as compared with its predecessor of 1896. The chief additions have been chapters upon retroversion of the pregnant uterus and upon puerperal eclampsia.

The apology made for their introduction upon the ground that they are not complications of labor is unnecessary, since both at times do complicate the child-bearing process, and, in any event, are closely related to it. The first of these two chapters may be dismissed with the statement that it is in keeping with the remainder of the work, than which no criticism could be more favorable; but this cannot be said with respect to the chapter devoted to eclampsia. This portion of the book is hardly abreast with present-day teaching, and a careful reading will leave one with a suspicion that the author did not desire that it should be. Aside from its last paragraph, consisting of instructions as to treatment by morphine and hydrotherapy, it is somewhat too vague to be of much practical value, both as regards pathology and treatment. While it is universally admitted that our ignorance as to the essential etiology of eclampsia is abysmal, it would certainly have served a better purpose to have considered the subject from the basis of the theories of auto-intoxication rather than to have made a thoroughly artificial division, admittedly based upon an imaginary pathology. The most glaring defect in the chapter, however, is the hopeless attitude with regard to prophylaxis. This is pernicious teaching in the light of common present-day knowledge. It is to be hoped that in the editions of the future the author will see fit to bring this chapter up to the standard of excellence of the remainder of the work. W. R. N.

Practical Obstetrics. By E. Hastings Tweedy, F.R.C.P.I., Master of the Rotunda Hospital, Dublin; and G. T. Wrench, M.D., Late Assistant Master. Second edition; pp. 491; 159 illustrations. London: Henry Frowde, and Hodder & Stoughton, 1910.

This book, as is shown by its title, aims to present simply the practical side of obstetrics. It is really a rather elaborate compend or syllabus, as those terms are understood in this country; in other words, it is a book which will be useful to the student preparing for examination or to the ill-trained practitioner who desires to become conversant with the elements of obstetrics. It could not be used as a text-book in American medical schools of the first class, as it comprises simply the practice of the Rotunda Hospital and does not pretend to give an exhaustive survey of either the theoretical or practical aspects of the subject. Its review has been of decided interest, since it is an authoritative expression of the technique of a very famous institution. Of course, it goes without saying that in the main its teaching is the result of great experience and that it is eminently sound, but there are a few exceptions. For instance, we have been greatly interested in the advised avoidance of both bleeding and sweating in the treatment of eclampsia; in the statement

that patience is the only treatment of an undilating os, the result of primary inertia; and the implied advocacy of quinine, ergotinin, and treacle as stimulants in uterine inertia. While by far the greater number of subjects are well and clearly handled, the description of vaginal Cesarean section and uterine suspension are not given in sufficient detail to allow of their comprehension by the ordinary reader. The advocacy of complete anesthesia for forceps delivery is certainly dangerous teaching if followed by the general practitioner in his every-day practice. Those who follow it conscientiously will undoubtedly gain a rather wide experience in postpartum bleeding. It seems rather foolish to advocate the use of the Skutsch pelvimeter to men whose work is of necessity done in private houses and in many instances among the poor. This instrument is undoubtedly of value in trained hands, particularly in hospitals where ample assistance is available, but the ordinary practitioner would certainly obtain naught but misleading evidence from its use. The usual method of estimation by means of the diagonal conjugate as measured by the examining finger is amply sufficient for his needs. In the performance of abdominal Cesarean section it hardly seems needful to compress the broad ligaments during the incision of the uterus or to dilate the cervix afterward, even if there were no dilatation. Certainly the use of the finger as the dilating force would not appeal to many obstetricians.

While, as has been already stated, the book fulfils its purpose quite well, it is nevertheless somewhat of a disappointment, since a different treatment of "practical obstetrics" might be expected from men of the prominence and experience of the authors of the present volume. W. R. N.

Medical Electricity and Röntgen Rays, with Chapters on Phototherapy and Radium. By Sinclair Tousey, A.M., M.D., Consulting Surgeon to St. Bartholomew's Clinic, New York. Pp. 1116; 750 illustrations. Philadelphia and London: W. B. Saunders Company, 1910.

Like other books written upon electricity, it first deals with general considerations and principles, and then takes up the special currents.

The illustrations are good. The book is well gotten up, and it is indeed a welcome sight to see new plates for motor points and not the old Erb plates, which are used in practically every text-book.

It is difficult to review a large work of this kind, but the first impression is that the book is rather too large. Not that comprehensive treatment is out of place, but there is a lot of repetition of theories by other authors, not only of general principles, but of therapy, and the consequence is that many statements are made of cures of diseases by different forms of electrical application which are

not borne out by facts, but which the author quotes in good faith from men who apparently should know. The truth of the matter is, that no one person is qualified to write upon all the different phases of electricity and its treatment. A man who devotes his time to *x*-ray work cannot very well be expert in the general treatment of nervous diseases by electricity, and the same thing holds true for the neurologist.

The reviewer is a neurologist, and therefore can only review the book from his standpoint. For example, in the treatment of scleroderma the statement is made that "perforating ulcer of the foot has been cured by faradization of the posterior tibial nerve and erythromelalgia and symmetrical gangrene have been successfully treated by the local application of galvanic currents." This is a rather strong statement, and one which the reviewer wishes were true. Again, the statement is made that a "galvanic hydroelectric bath for sciatica cures the majority of the cases." Every neurologist is at times compelled to use electricity in the treatment of neuritis, but unfortunately not always with good results. It is difficult to understand why manufacturers of electrical apparatus always persist in having their electrodes covered by sponges when a metal disk with cotton is so much better and cleaner, and yet in most of the illustrations sponge electrodes are shown.

The chapter on nervous diseases is particularly well done, and the description of the various palsies, disturbance of sensation, etc., is up to date, and is to be commended. One is interested in seeing a description of Laduc's treatment of trigeminal neuralgia by means of cataphoresis, and the author is correct in rather doubting its efficacy.

It is rather difficult to understand the following. In discussing the value of high-frequency currents, the author states that he has had some success in the treatment of infantile paralysis, and then he mentions the following extraordinary case on page 542: "One poor little hand was crippled and about one-half the natural size, and the leg on that side was in about the same condition. A few months' treatment with a vacuum electrode connected directly with one pole of an *x*-ray coil brought the paralyzed arm and leg up to a size exceeding those of the normal limbs originally, and at the age of two and one-half years the boy weighed forty pounds, and was strong and jolly." He further recommends high-frequency treatment for epilepsy, chorea, and locomotor ataxia, stating that in the latter disease such marked improvement resulted in a case that "the patient's friends have stopped him on the street and asked him what treatment he was receiving." Such statements do not sound well.

Since the introduction of the *x*-rays in 1895 the advances made in it are remarkable, and the author discusses this part very well. The plates are excellent. On the whole, the book is good, and the author should be commended for his work.

T. H. W.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

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A Sulphur Reaction in the Urine in Cancer.—H. Solomon and P. Saxl (*Wiener klin. Woch.*, 1911, xxiv, 449) have made a further study of the oxyproteinic acid of the urine in carcinoma. It is fairly rich in incompletely oxidized sulphur, and Solomon and Saxl have devised a method for oxidizing the sulphur and determining the approximate quantity of sulphate resulting. The method is as follows: 150 c.c. of urine are diluted with 100 c.c. of distilled water. (Albuminous urines must first be boiled, acidified with dilute acetic acid, and filtered.) One then adds 150 c.c. of baryta mixture to remove the sulphates (Salkowski). Baryta mixture consists of two parts of a solution of barium hydroxide saturated at room temperature and one of barium chloride, also saturated at room temperature. (The salts must be chemically pure and kept in stoppered bottles to prevent efflorescence. The saturated solutions are filtered clear.) After adding the baryta mixture, filter and test a small portion of the filtrate with a few drops of baryta to see whether precipitation has been complete. Then, to remove the ethereal sulphates (according to Salkowski), 300 c.c. of the filtrate are taken, to which 30 c.c. of HCl (sp. gr. 1.12) are added, and the whole placed in a 500 c.c. Erlenmeyer flask. The latter is covered with a small funnel, placed on asbestos and boiled one hour over a small flame. (One must guard against change in the HCl concentration from this point onward, hence the use of the funnel in the mouth of the flask.) After boiling, the flask is covered with

a beaker and placed on the water bath, where it remains till the fluid overlying the precipitate is clear, usually four to twenty-four hours. Now one filters twice through a double, dry baryta filter (Baryt-filter)—use a small filter—washes the Erlenmeyer flask with alkali, water, and distilled water, and then boils again for a short time in the same flask with the funnel in place. Again one filters through a double baryta filter. (If a precipitate remains on the filter, the flask is returned to the water bath.) Two hundred c.c. of the filtrate are now treated with 3 c.c. of Merck's perhydrol (hydrogen dioxide) and boiled one-quarter of an hour in the same Erlenmeyer flask with the funnel in the neck. After boiling, the fluid is poured into a conical sedimenting glass, and within one-half to four hours one sees a precipitate settling to the bottom. This precipitate is abundant only in cancer. Ordinarily, in normal urines there is no precipitate, or at most a trace within four hours. Usually, much later a precipitate appears, which is possibly barium sulphate derived from the ethereal sulphates. The precipitate in cancer is barium sulphate plus pigment; the latter is removable by extraction in alcohol-ether. What remains is sulphate obtained by oxidation from the neutral sulphur. Solomon and Saxl have tested the urine from 81 cases of cancer, of which 61 gave a markedly positive reaction, 10 weakly positive, and 10 negative. A negative result was obtained in 79 controls. Three cases which were positive remained clinically doubtful, being apparently myoma uteri, pseudoleukemia, and anemia gravis. The reaction may appear early, even with very small tumors, and appears to be practically specific.

Diagnostic Value of the Butyric Acid Test (Noguchi) in Cerebrospinal Fluid.—In the routine study of all spinal fluids sent to the laboratory of the Michael Reese Hospital for diagnosis, STROUSE (*Jour. Amer. Med. Assoc.*, 1911, lvi, 1171) has studied particularly the status of the butyric acid globulin test as devised by Noguchi. In 5 cases of cerebrospinal syphilis, and in 7 of general paresis, he found the Noguchi test positive. In 2 cases of tabes the test was positive, and in 2 negative. The Wassermann test in the blood of one of the latter was positive. In contrast to this series are 3 cases of brain tumor, 2 of dementia præcox, and 2 of cerebral arteriosclerosis, in all of which the Noguchi test was negative. As an aid in the differential diagnosis between acute meningitis and other inflammations of the meninges, Strouse found the test positive in 4 cases, 1 each of pneumococcus, meningococcus, streptococcus, and influenzal meningitis. In contrast is a negative test in 3 cases of meningismus, 2 in pneumonia, and 1 in typhoid fever. He found positive Noguchi reactions in 18 cases of tuberculous meningitis, all of which later gave a positive diagnosis by the finding of tubercle bacilli or by autopsy. The test was more constant than lymphocytosis and was much easier to perform than a total or differential cell count. In 9 cases in which the tentative diagnosis of tuberculous meningitis had been made, the test was negative and the later course proved the diagnosis to be incorrect. Warning is given, however, that even in clinical conditions which may resemble tuberculous meningitis a positive reaction does not by any means indicate the presence of a tuberculous inflam-

mation. A negative one presupposes the absence of such a condition. He concludes that the tests for increased globulin in the spinal fluid are easier to perform than the total cell count, and have practically the same diagnostic importance. The butyric acid test of Noguchi is convenient, accurate and gives information of considerable value in diagnosis. He employed the test as follows: One part (0.1 or 0.2 c.c.) of cerebrospinal fluid is placed in a test-tube and to this is added 5 parts of a 10 per cent. solution of pure butyric acid in physiological salt solution; the mixture is heated to boiling and immediately one part of normal sodium hydrate added and the mixture again boiled. In the presence of increased globulin a definite flocculent precipitate occurs, either immediately or within two hours. This definite precipitate must be differentiated from a faint cloudiness which normal fluids may give, but it requires only slight experience to recognize the difference between positive and negative reactions.

Peptid-splitting Ferment in the Saliva.—The glycyltryptophan test for the diagnosis of gastric carcinoma, as described by Neubauer and Fischer and the results obtained by Lyle and Kober, and by Weinstein, have been reported in previous numbers of this journal. A striking feature of their reports has been the consistency with which the reaction has stood the test of application. In the presence of anacidity and the absence of pancreatic juice and blood, the stomach juice which has split the polypeptid glycyltryptophan has been said to contain a proteolytic enzyme derived from carcinoma. Warfield (*Johns Hopkins Hosp. Bull.*, 1911, xxii, 150), dissatisfied with discordant results, investigated the effect of saliva upon glycyltryptophan and was surprised to find the presence of an enzyme which split tryptophan from the dipeptid. This enzyme is destroyed by heating to 100° C. and is not active in acid saliva. Warfield explains the presence of the test in achylia gastrica by the presence in an alkaline medium of swallowed saliva. An occasional acid saliva would explain an occasional negative test. When the stomach contents are acid, 0.05+ per cent. the test is negative. Warfield acknowledges the presence of a peptid splitting enzyme in the cancer juice, but points out that the absence of free hydrochloric acid in the stomach contents in cases of carcinoma presents a condition most favorable for the action of the salivary peptid splitting enzyme. He has not determined from what glands, parotid or submaxillary and sublingual, this enzyme was secreted. He has not determined the effect of the bacteria in the saliva. In view of these facts, he concludes that the glycyltryptophan test is of no value in the diagnosis of cancer of the stomach.

Cardiac Insufficiency, Albuminuria, and Cylindruria Caused by Chronic Coprostasis.—Ebstein (*Münch. med. Woch.*, 1911, lviii, 615) reports his clinical findings in several recent cases. His observations have led him to believe that when the cardiac resistance as determined by tactile percussion is widened, one possibility to be considered is dislocation of the heart from a high position of the diaphragm. If such be the case, the cardiac symptoms, which may amount to a muscular insufficiency, may be cured if it is possible to cause the

diaphragm to return to the normal level. Chronic coprostasis is a frequent cause of elevation of the diaphragm. Again, before giving an unfavorable prognosis because of albuminuria and cylindruria, one must relieve a chronic constipation, since both may disappear with the establishment of normal fecal evacuations.

A New View of the Function of the Renal Glomerulus.—Brodie (*Jour. Can. Med. Assoc.*, 1911, i, 18) discusses a new view of the function of the renal glomerulus. On the assumption that the glomerulus discharges the bulk of the water and does actively secrete, he says that, since the abandonment of the filtration hypothesis, there has been no explanation of the function of this characteristic and peculiar structure. He feels that the glomerulus actively sets up a pressure head whereby the column of fluid is propelled along the tortuous tubule; for it seems reasonable to suppose that a considerable head is necessary to force fluid through the tubule, as it is a capillary tube. He observed the rate of flow from a dog's kidney in active diuresis; ligated the vessels; fixed the organ in formalin, and found out the number of glomeruli in each kidney, thus getting an idea of the rate of flow from each tubule. From the law of motion of fluid in a tube of that diameter he found the average glomerular pressure to be about 95 mm. Hg. All attempts to show that any renal cells can give an excretory pressure similar to that of the salivary glands failed, and consequently we must assume that the pressure just outside the glomerular tuft is the same as the renal capillary pressure. This renal capillary pressure is about 30 mm. Hg., less than arterial pressure, that is, 95, the same as found necessary to propel the fluid through the tubule. The popular view explains many facts brought to the support of that of filtration, that is, why the tuft has the firm unelastic Bowman's capsule and why the afferent vessels are larger than the efferent. This arrangement permits of a rapid enlargement of the glomerulus without loss of pressure. Nussbaum has described a pulsation of the glomerulus in the newt, and the tubules in active diuresis have been found increased in length. Both of these conditions are due to increased glomerular pressure. Furthermore, it has been found that the urinary secretion ceases at a pressure of about 30 to 40 mm. Hg, lower than the arterial pressure, that is, when the urinary pressure equals that in the glomerulus. Caffeine diuresis has been ascribed to the vessles alone, but proof is now at hand that caffeine products exercise a marked influence on the renal cells, and that under their influence the cells become incapable of holding back chlorine from the blood, after the chlorine content has fallen below normal. Then experiments on the frog's kidney where glomeruli and tubules have a distinct circulation leave no doubt that under caffeine diuresis, the tubules secrete, hence, in nephritis, great care should be taken in caffeine administration.

The Sensibility of the Alimentary Canal in Health and Disease.—Hertz (*Lancet*, 1911, clxxx, 1051), in the Goulstonian lectures, records his observations on the sensibility of the gastro-intestinal tract to various stimuli. The mucous membrane of the whole canal was found insensitive to tactile stimuli; that of the stomach and intestines alone was insensitive to thermal, the esophagus and rectum being sensitive.

The esophagus and stomach are quite insensible to dilute hydrochloric acid even as high as 5 per cent., a concentration never found in health or disease. Glycerin affects the anal canal, and alcohol generally produces a feeling of warmth. The feeling of fulness in stomach and intestines is due to a slow increase in the tension exerted on the muscular fibers of their coat. The volume of contents necessary to produce this tension varies with the tone of the organ, that is, a small quantity will cause a sensation of fulness in a tonically or organically contracted stomach, while it would be unnoticed in the dilated. In the rectum this special sensation of fulness is a "call to defecation." This call should be answered at once; for the passing off of the desire is not due to a return of the feces to the pelvic colon, but to a gradual relaxation of the rectal wall. A new desire means only one thing—that more feces have come to the rectum, and to prevent progressive dilatation it should be evacuated at once. The feeling of hunger is one of general malaise associated with the periodical muscular activity of the stomach when empty and the nerves hypersensitive. This causes local pressure symptoms analagous to those to be described in pain. Hunger can be allayed by the taking of water or of any non-digestible substance like earth. It is, however, with especial reference to abdominal pain that his observations are most interesting. He has described how he found the stomach insensitive to hydrochloric acid, even when ulcerated, and believes that abdominal pain is, in part, truly visceral and has one cause —tension produced upon the muscular coat of the viscus. This tension must be induced rapidly; if slowly the sensation of fulness results, and the pain returns when more pressure is added. Gastric pain associated with ulcer he describes as due to the pressure caused by (1) pyloric spasm either organic or due to the passage of too acid chyme into the duodenum, together with (2) increased peristalsis of the pyloric end of the stomach. This rapidly raises pressure locally, and the pain is severe. The peristalsis may be more active from direct stimulation of the nerves of the open ulcer, or it may be due to plain hyperacidity. If the ulcer is in the cardia, the peristalsis is evidently greatly increased, reaching a region of the stomach where it normally does not belong. The late pain of duodenal ulceration he explains by the fact that the first chyme to pass the pylorus has hydrochloric acid bound with the protein, and that there is no excess to cause pyloric spasm. As the secretion of hydrochloric acid rises, the spasm increases and peristalsis causes the rise in pressure. Relief by soda bicarbonate is explained by the reduction of acidity and consequently of the pyloric spasm, thus permitting extrusion of chyme. Similarly, vomiting results in emptying of the stomach with lack of pressure owing to their being nothing for the stomach to contract upon. The pain in chronic appendicitis and cholilithiasis is most probably due to reflex inhibition of the pyloric relaxation. That of colic is due to increase of pressure caused by excessive peristalsis and spasm of the next lowest colonic segment. Local tenderness may be due to two things—hyperalgesia of the skin, subcutaneous tissues, and muscles, together with a local rise in tension, caused by the pressure of the hand. That it is not due to pressure on the ulcer is evident from the fact that exploratory laparotomies often show the ulcer to be remote from the tender spot.

The Relationship of Electrocardiographic Methods to Medicine.—Lewis (*Proc. Roy. Soc. of Med.*, 1911, iv, 81, medical section) discusses the relationship of electrocardiographic methods to medicine. Its principal work has been to clear up the mystery surrounding delirium cordis and paroxysmal tachycardia. The delirium cordis is definitely due to the experimentalists' fibrillation of the auricles, and this is accountable for 50 per cent. of all irregularities; it is of further importance because it reacts to drugs in a specific manner. Cases of paroxysmal tachycardia may be placed in several classes. The first show crises of auricular fibrillation. In the second the paroxysms depend upon new impulse formation in the myocardium at a point remote from the normal impulse formation area; the attack depends upon the substitution of a new rhythm for the old. With this discovery has come the localization of the pacemaker in the right auricle just at the entrance of the superior vena cava. While the instrument lacks the portability of the polygraph, it can be carried remotely by wires, and it gives quickly an infallible analysis of the sequels of contraction in the cardiac chambers (not of the effects of contraction on the veins, as does the polygraph) without any measurement. Finally it gives information of the direction pursued by the contraction waves. It must be given a place with percussion and auscultation. Its information is direct and definite whether given or withheld.

The Behavior of Various Organic Acids Concerned in Diabetic Acidosis.—Labbe and Trolle (*Presse Méd.*, 1911, p. 284) have investigated upon rabbits the various organic acids supposed to be concerned in diabetic acidosis. After showing that mineral acids either killed quickly by intense action or could not produce coma, they tried propionic, lactic, butyric, and beta-oxybutyric acids successfully producing coma with all. Independent of the toxicity due to the acid, is a specific toxicity due to the chemical constitution, and those without the alcohol radicle are the more dangerous. One can diminish the first toxicity due to the acid by saturation of the animal with alkali, but the specific toxicity is not affected; for example, if it takes 375 grains of soda butyrate to kill an animal, the corresponding dose of acid is 90 grains. As this acid content can be neutralized, they believe in the free administration of alkalies, carbonate of soda preferably, and also in the exhibition of alcohol, since those with alcohol in the radical are the less toxic. Most failures are due to a failure of saturation by the alkali treatment.

Urobilinogenemia.—R. von Jaksch (*Münch. med. Woch.*, 1911, lviii, 746), in referring to the work of Hildebrandt (*Ibid.*, 1910, lvii, 2574), who claims to have been the first to demonstrate urobilinogen and urobilin in the blood serum, shows that the latter is mistaken and points to an earlier reference. Von Jaksch also states that for years he has observed urobilin in the blood serum in the lobar pneumonia. In his experience, urobilinogenemia has always been associated with severe, fatal infections. No hepatatitis has been found associated at autopsy. The serum from such a case, at first yellow, gradually assumes a greenish fluorescence on prolonged exposure to the light. No bilirubin has been demonstrable in the serum.

SURGERY

UNDER THE CHARGE OF

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Jejunal Ulcer after Gastro-enterostomy.—Exalto (*Mitth. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, xxiii, 13) says that since Braun, in 1899, demonstrated the occurrence of ulcer of the small intestine following a posterior gastro-enterostomy, only a relatively small number of cases has been reported. Probably many more occur, but because of favorable circumstances are healed. The known cases may be divided into those in which perforation occurs into the free peritoneal cavity, and those in which the ulcer adheres to the anterior or posterior abdominal wall and is thus encapsulated. All writers have discussed the diagnosis and therapy and especially the obscure etiology. Almost all have based their conclusions upon speculation without experimental evidence. Exalto performed a series of experiments on dogs with the object of studying the effect of the gastric juices on the jejunal mucous membrane. He concluded that the ulcer following gastro-enterostomy is the result of the effect of the acid gastric contents upon the intestinal mucosa. It remains undecided whether the lesions are due to mechanical trauma or other causes primarily present; or whether the chemical trauma is of too high a grade for the life of the epithelial cells of the mucous membrane. The Roux Y method of operation on the anterior or posterior wall, and those methods which are associated with a Braun anastomosis (entero-anastomosis), must be avoided. The method which affords the least possibility for the development of a jejunal ulcer, is the retrocolic posterior gastro-enterostomy (v. Hacker), as near as possible to the duodenum. The after-treatment for persons upon whom the operation has been performed for ulcer should provide for an ulcer diet for a long period, with the administration of alkaline substances, since this is an important factor in the prevention of jejunal ulcer.

The Anatomical Basis for Surgery of the Lymph Nodes; The Regeneration and New Formation of the Same.—Vecchi (*Mitth. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, xxiii, 42) says that conclusions based upon clinical observations have little support. Only experimental evidence has any value. Vecchi carried out a series of experiments upon dogs, and as a result concluded that after a total enucleation of a lymph node, no regeneration occurs. The symptoms which develop as a consequence of the operation (lymph effusion, scar formation,

edema, etc.) after varying periods of time disappear. The lymph circulation is carried on partly through preformed or new-formed collateral vessels, and in part through the old path which is in most part reëstablished. After a resection of a lymph node, regeneration of the resected portion never takes place. Healing occurs by the development of a scar. The behavior of the remaining portion of the node will depend upon the direction and extent of the resection. By the injection of certain substances into a lymph node, an experimental exuberance can be produced, such as occurs in certain pathological conditions (inflammations, malignant tumors). Under the influence of the long-continued irritation, the lymph follicles grow toward the periphery and form plugs and buds which project into the perinodular connective tissue. They may become detached from the node and form daughter nodes. These occur especially in the direction of the lymph stream, along the afferent vessels of the wounded lymph node. It is not an autogeneration but an outgrowth. By the formation of a connective-tissue septum in an altered node, the latter may be divided into two portions, which may be mistaken for newly formed nodes.

Suction Treatment in Sterile Sand Baths of Infected Wounds and Wounds Suspected of Being Infected.—Thiers (*Zentralbl. f. Chir.*, 1911, xxxviii, 458) has employed in many severely infected wounds, with much satisfaction, a method of treatment which is based upon the ability of fine sand to exert capillary attraction upon fluids. The finer the grains of sand the greater the suction. The suppurating wound or sinus is covered with sand until the involved portion of the body, as the forearm, lies in the sand bath. A quadrilateral tin box or gutter, with removable or very low ends, answers the purpose. The secretion is quickly drawn from the wound, so that the sand in the immediate neighborhood of the wound should be changed frequently. This the patient can manage with a spoon. To sterilize the sand it should be placed in a linen bag holding about 3 to 4 liters of sand, with the neck of the bag tied; it should be placed in a suitable vessel, filled with a 1 per cent. soda solution, and boiled about a half hour. The alkaline reaction of the sand will prevent the clotting of substances from the wound and the tendency to scabbing. The sand should be sterilized daily or every two or three days. The development of a putrid odor in the sand will call for frequent changing of it. Frequently the application of the sand bath for twelve to fourteen hours will be sufficient. If during the night marked swelling and redness return, a re-immersion in the sand bath will cause them to disappear, frequently in two to three hours. Occasionally the suction is so strong and the discharge so free, that the patient becomes exhausted, and the bath must be discontinued after a short period. In such a case Thiers found it necessary to remove the wound from the bath from time to time and to employ sand with larger grains. For this treatment are found most suitable, large wound surfaces with marked infiltration, wounds with flabby and hypertrophic granulations showing no tendency to cicatrization, and putrid infections with much secretion and showing much edema. The edema and inflammation quickly disappear, the granulations become full and bright red, and the cicatrization progresses favorably. The pain also disappears in a similar manner and the

mobility of joints is improved. The sand bath is particularly suited to the treatment of gangrenous and severely traumatized tissues, the infection being also combated by the usual antiseptic measures, iodoform, etc. The method is also suited to the after-treatment of skin grafting. The grafts can be covered by a fine wire netting which may be fastened to the surrounding skin by collodion. The part is then placed in the sand bath, the fine netting holding the grafts firmly to the wound surface. The part may be taken out of the bath at night and the netting covered with a dry compress without attempting to wash away the sand which has passed through the netting on to the wound surface. On the following morning the compress can easily be removed.

The Operative Treatment of Varicocele.—Nilson (*Zentralbl. f. Chir.*, 1911, xxxviii, 597), during a service of seven years in a marine hospital, treated 65 seamen suffering from varicocele. All of these, with one exception, were operated on at their own request, on account of pain. In only the one case was the operation performed on account of sexual disturbances, which does not agree with the generally accepted opinion on this point. Nilson did the operation in the inguinal canal because he could better avoid the spermatic artery and, therefore, any resulting interference with the nutrition of the testicle. The constituent structures of the spermatic cord can be easily seen in this situation. It has been shown that if in operations in which a portion of the pampiniform plexus is excised, the stumps are brought together in direct contact, the vessels unite and a secondary reëstablishment of the lumina may occur from the vasa vasorum. Recurrences of the varicocele, however, are frequent. In his cases Nilson did the following operation: An incision was made along the inguinal canal as in the Bassini operation. When the external spermatic vein was varicose, a piece of it was excised. The internal spermatic vein, into which the pampiniform vein empties, was isolated and ligated high near the peritoneum. The lower vein stump was then separated below from its sheath, which is easily done because no branches are given off. It was then drawn upward until the testicle was felt near the symphisis pubis. In order to fix the testicle in this position, the long lower vein stump was passed between the lower bundles of the aponeuroses of the internal oblique and transversalis muscles and tied in a knot around the lower separated bundles. This knot was further secured by suturing the end of the vein stump to Poupart's ligament. The external oblique and the skin and fascial wounds were then closed by suture. The ends of the two vein stumps are so separated that a reestablishment of the blood paths is out of the question and the testicle is securely suspended. The operation can be performed in fifteen minutes and under local anesthesia without pain, the ilioinguinal and external spermatic nerves being injected with cocaine. Thirty-seven cases were later investigated; 2 after six years; 3 after three to four years; 3 after two to three years; 5 after one-half to one year; and 21 after three to six months. Thirty-three were completely cured; 3 were much improved; and only one after seven months was not free of pain. All those which were not investigated were discharged from the hospital, free of symptoms after a two weeks' convalescence.

The Prognosis of Dislocations of the Shoulder and of Posterior Dislocations of the Elbow.—Schmidt (*Deut. Zeitschr. f. Chir.*, 1911, cix, 20) investigated the material treated in the Kiel surgical clinic from 1900 to the end of 1908. Schulz had already reported on similar investigations from Küttner's clinic at Breslau, and had found the results very unsatisfactory. Schmidt found that 92 cases had been treated in the Kiel clinic in the time stated, of which 56 could not be located, and 9 others excluded because of complications such as fractures, paralyses, and recurrent dislocations. There remained 27, in 22 of which the final results were very good. A limitation of abduction of five to ten degrees was disregarded, as it was found to amount to practically nothing in interfering with the usefulness of the arm. There were 6 of these, and the patients were well satisfied with the results. Crepitation in the joint, without limitation of movement or other disturbances, was found in 26 per cent. of the cases. Slight atrophy of the scapular muscles or of the deltoid was found in 29.6 per cent., but the results were otherwise good. Atrophy was present in all the cases with bad results, with one exception. The age of the patients had nothing to do with the prognosis. A good result was obtained in 81.4 per cent. of the cases. In those cases in which the results were poor, the after-treatment was begun after two to three days and consisted in massage, gymnastic exercises, and methodical exercises with medico-mechanical apparatus. The best treatment consisted in keeping the shoulder at rest for ten to fourteen days, by a sling from the wrist and fixation with a loose bandage. Gentle massage was employed to improve the circulation and favor absorption of the extravasated blood. With this treatment the prognosis of an uncomplicated dislocation of the shoulder should be regarded as favorable. With regard to the posterior dislocations of the elbow, the general tendency to give a good prognosis is hardly justified. Forty-six cases had been treated from 1900 to 1908, inclusive. Four of these were excluded because of various complications and 22 more because they could not be located. Of the 20 remaining, 1 was unreduced. Of the 19, in 13, or 69 per cent., the return of function was complete, except for about 10 degrees of limitation of flexion and extension, which was not regarded as interfering with the usefulness of the arm. In 4 cases the disturbances were serious in all the movements of the elbow-joint, in 1 the ankylosis being complete. Schmidt warns here, as in the shoulder, against too early and too energetic therapy, and advises rest of the joint for about the first two weeks.

A Contribution to the Question of Coxalgia, Coxa Vara, and Juvenile Osteo-arthritis Deformans.—Levy (*Deut. Zeitschr. f. Chir.*, 1911, cix, 205) says that a coxalgia can be associated with an existing coxa vara and a picture of a contracted coxa vara may be presented. After an epiphyseal separation in a tuberculous individual with coxa vara, a tuberculous infection can arise secondarily in the hip-joint at the site of the focus of lessened resistance. Before attempting to correct forcibly a coxa vara, the possibly existing tuberculous coxitis must be excluded with certainty. When lung tuberculosis exists in a case of coxa vara, forcible correction should be avoided as much as possible. The affection designated as juvenile osteo-arthritis deformans is not

the same as the usual arthritis deformans. It is due to disturbances in the region of the epiphyseal cartilage, just as in coxa vara. The great clinical and anatomical similarity between these two conditions justify the name of coxa vara capitalis in the place of juvenile osteo-arthritis deformans. A large percentage of the cases of so-called osteal tuberculosis of the hip-joint, which are cured with normal or very good mobility, are really not tuberculous, but cases of coxa vara capitalis.

Injury as a Causative Factor in Cancer.—Coley (*Annals of Surgery*, 1911, liii, 615), as the result of a careful study of the evidence based upon 1200 personal observations, believes that local trauma, from chronic irritation to a single local contusion, is not infrequently the direct exciting cause of malignant tumors of all types. That a single local injury may cause a carcinoma as well as a sarcoma is no longer open to speculation. The cases that he has submitted fulfil all the conditions necessary to establish a definite casual relationship between a single trauma and the development of a cancer. This relationship depends in no way upon our ability to offer a scientific explanation for it; nor does it depend upon the acceptance of any one of the various hypotheses as to the etiology of cancer. It can be equally explained, whether we accept the extrinsic or intrinsic origin of malignant tumors. The medicolegal aspect of this question is as yet in a most unsettled state. While we must admit that trauma often plays an important causative role in the formation of malignant tumors, this relationship must be clearly and definitely established, according to principles and conditions very similar to, if not quite so exacting as, those laid down by Segond, before any legal liability can be admitted.

Gastro-enterostomy as Shown by the X-rays.—Härtel (*Deut. Zeitschr. f. Chir.*, 1911, cix, 317) says that while the physiology after gastro-enterostomy has been thoroughly studied in animals, the conclusions drawn from such studies cannot be applied with force to ulcerated stomachs in men. Härtel made his studies in patients with particular reference to the late results. Some were studied four months after operation, some as late as three years, the average being one and one-half years. All of them had suffered from benign affections of the stomach. Twenty-two cases were thus studied with the aid of the *x*-rays. The anastomotic opening participated in the evacuation of the stomach in every case, the pylorus in only a part of the cases. The bismuth food introduced into an anastomosed stomach was retained until it filled the stomach entirely. Gradually the evacuation took place, beginning earlier and being earlier completed than in a normal stomach. Aside from that which took place through the pylorus, the evacuation occurred periodically and synchronously with the peristaltic movement of the body of the stomach. Without the development of a new sphincter apparatus, a gastro-enterostomy acts in a manner similar to the physiological action of the pylorus. It does not work as nicely as the pylorus, but has something of the relation to it that a deficient heart opening has to a normal one, and can be seriously crippled if the open pylorus works vigorously. The kind of pathological process affecting the stomach may involve the mechanism of evacuation after a gastro-enterostomy. This evacuation through the gastro-

enterostomy opening is not purely a mechanical process according to the law of gravity; but is influenced by the physiological laws of the stomach movements. The capacity of the stomach for active movement exceeds that necessary for evacuation through the gastro-enterostomy opening, and is capable of increasing the tone of the stomach in ectasia after gastro-enterostomy. The prognosis depends in good part upon the indication for operation. Other factors affect it, especially accessory diseases, by causing later troubles. The mechanism of evacuation is also affected by the indication for the gastro-enterostomy, since the activity of the pylorus is important for the later function. When it is done for a stenosed pylorus, the new opening, while not ideal, for practical purposes fulfils the role of the pylorus. Spastic conditions of the pylorus are relieved by gastro-enterostomy. When it is done for an ulcer of the middle portion of the stomach, it frequently happens that the food is not diverted sufficiently through the new opening and in great part goes through the pylorus as before the operation. Frequently internal treatment will be necessary after the gastro-enterostomy.

THERAPEUTICS

UNDER THE CHARGE OF

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The Treatment of Acidosis.—Lichtwitz (*Therap. Monatshefte*, 1911, xxv, 81) advocates sodium citrate in place of sodium bicarbonate for the treatment of acidosis. He says that sodium citrate is practically tasteless and may be added to food and also given dissolved in water with the addition of lemon juice. When given this way it makes a very pleasant drink. Sodium citrate causes much less disturbance to the digestion than sodium bicarbonate. He has given sodium citrate up to 50 grams a day, and it has not caused diarrhea, that sometimes results from large doses of sodium bicarbonate. He also adds that it is theoretically possible to give sodium citrate solution by subcutaneous injection, while the strong alkaline reaction of a sodium bicarbonate solution prevents its use subcutaneously. However, he has had no personal experience with subcutaneous injections of sodium citrate.

Silver Nitrate Irrigations in Treatment of Infectious Diarrhea in Children.—Smith (*Boston Med. and Surg. Jour.*, 1911, clxiv, 298) writes concerning the treatment of infants ill with infectious diarrhea by colon irrigations of 3 per cent. silver nitrate. A cleansing irrigation with sterile water is given before the silver nitrate solution. After the preliminary cleansing has been completed, one pint of a 3 per cent. silver nitrate solution is allowed to run into the colon and the tube

then withdrawn. Some of the solution is retained. Smith says that there was no marked evidence of discomfort following the injections. Thirty-two cases were treated by this method. Three infants showed a rather severe temporary reaction. These infants were very sick, and Smith doubts if the reaction was any greater than it would have been had they received the simple irrigation without the subsequent silver nitrate injection. The treatment was given early in the disease in 22 cases; 11 of these were markedly improved and 7 slightly; 3 out of 6 patients who received the treatment late in the disease were benefited. Smith believes that blood and pus disappear from the stools more rapidly and that the course of the disease is shortened.

The Vaccine Treatment of Typhoid Fever.—Walters and Eaton (*Med. Record*, 1911, lxxix, 797) report 35 cases of typhoid fever treated by vaccines. This report supplements previous communications, in which they claimed that the vaccine treatment of typhoid fever reduced the mortality, shortened the length of the disease, and rendered relapse less liable to occur. They give a brief synopsis of any unusual features of each case, with the accompanying temperature charts. No aggravation or injury of any kind was demonstrable as a result of any inoculation. They believe that small dosage is an important factor in successful treatment particularly in making the second and subsequent inoculations somewhat smaller than the first. The more serious the clinical condition of the patient the smaller the dose employed. This was apparently shown in one case that was considered to be all but hopeless. Here daily doses of one or two million bacilli were followed by a gradual change for the better in the clinical symptoms.

An Analysis of the Clinical and Serological Results Obtained in the Treatment of Syphilis with Salvarsan.—Fordyce (*New York Med. Jour.*, 1911, xciii, 861) reports 175 cases of various stages of syphilis treated with salvarsan. He is firmly convinced that this remedy is of great value, although the original claim of a therapia sterilisans magna is no longer entertained by those most familiar with its use. Fordyce believes that the chief question to determine at present is the standardization of its method of administration. It has now been quite conclusively established that a repetition of the dose in practically all stages of the disease is desirable. He recommends the following procedure for the treatment of syphilis: An intravenous injection followed by a course of mercurial inunctions or injections over a period of from four to six weeks. At the expiration of this interval a second intravenous injection of salvarsan and a subsequent course of mercury. At the end of this treatment a rest of a month and a Wassermann reaction. If it is negative, the patient is observed for one or two months and a second serum reaction is made. As long as it continues negative no treatment is indicated. Should it become positive a third intravenous injection of salvarsan supplemented by a course of mercury would be the best procedure to adopt. It seems to Fordyce that this method offers to the patient a far better chance of a rapid and permanent cure than the use of mercury alone. Should the reaction become negative after a single injection of salvarsan, it may be well to act on the advice of Ehrlich and repeat the injection, because of the possibility

of incomplete sterilization with the encapsulation of a few spirochetæ in the bony canals and the danger of recurrence in the nerves of special sense. Fordyce says that the aim of all treatment is to bring about a clean and clear negative Wassermann reaction which continues so for about a year. He believes that the majority of patients are inefficiently treated and that their treatment is not sufficiently controlled serologically. Fordyce thinks that the following conclusions are justified from his experience with salvarsan: In the primary and secondary stages of the disease two doses of salvarsan combined with active mercurial medication materially shortens the duration of the disease. The remedy certainly limits the contagious period of the infection, and in malignant cases its effects are nothing short of miraculous. It produces a rapid healing of the existing lesions, increases the patient's appetite, and improves the body nutrition. It is possible that in such cases we have a different strain of organisms which are more easily influenced by salvarsan than by mercury or potassium iodide. It is rather paradoxical, but it is nevertheless true, that the more serious the case and the more cachectic the individual, the more rapid are the effects of salvarsan. From a study of this disease extending over a period of thirty years Fordyce believes that he has seen more rapid and brilliant results from salvarsan in this class of cases than he has ever seen from the administration of the classical drugs.

The Use of Digipuratum in Heart Disease.—Boos, Newburgh, and Marx (*Arch. Int. Med.*, 1911, vii, 551) report their experiences with the use of digipuratum in cardiac disease. Digipuratum is a purified product derived from digitalis leaves with the elimination of digitonin, that is responsible for the irritant action on the gastro-enteric tract. This purified digitalis extract is a yellow liquid. It is standardized physiologically and is then taken up with sugar of milk to form a powder. The powder obtained is further diluted with sugar of milk until the resulting product has a definite and constant pharmacological strength. For greater convenience of dosage digipuratum is usually dispensed in tablet form, each tablet containing 0.1 gram of the powder corresponding to the average strength of a single dose (0.1 gram) of the crude powdered leaves. These tablets have an agreeable vanilla flavor and are taken readily by all patients. Digipuratum has now been in use at the Massachusetts General Hospital for over a year, and more than 180 cases of primary heart disease or secondary cardiac involvement have been treated with it. The effect on the urinary output has been very prompt in most instances. There was not a single case of vomiting or diarrhea; in fact, the vomiting of a number of cardiac patients at entrance was promptly stopped by digipuratum. Cumulative poisoning has never been observed. In one or two instances sudden drops of forty or more beats in the pulse rate occurred, but no disagreeable consequences followed in any case. It must be borne in mind, however, that digipuratum is a digitalis preparation, and that as such must necessarily have a tendency to produce poisoning by cumulation. In the case of digipuratum this tendency is merely much diminished, so that it is possible by means of this drug to push digitalis therapy in a manner heretofore unknown. This preparation has the advantage of being a more stabile preparation than other digitalis preparations and consequently dosage is more accurate.

A Safe and Rapid Method for Antityphoid Vaccine.—Fletcher (*Jour. Amer. Med. Assoc.*, 1911, lvi, 1016) describes in detail the method of administering antityphoid vaccines in the United States Army. In brief, the method consists in making three subcutaneous injections, at ten-day intervals of a Rill culture of Bacillus typhosus. The vaccine is contained in sealed ampoules, the standard content being 1,000,000,000 dead bacilli per cubic centimeter. The injections are made in the posterolateral aspect of the arm. The initial dose is 0.5 c.c. and the two succeeding doses are 1 c.c. each.

The Injection of Drugs, Especially of Salvarsan, into the Lumbar Muscles.—Meltzer (*Med. Record*, 1911, lxxix, 515), on the basis of experimental observations, suggests that injections of drugs, especially salvarsan, should be made into the sacrospinal muscle. He believes that such injections are practically not inferior to intravenous injections. He says that the sacrospinal muscle presents anatomically an exceptionally well isolated large compact mass, densely packed with fine muscle bundles. Any solution or suspension injected strictly into the mass will remain there and not affect locally the adjacent tissues. Experimentally it was shown that the absorption from the muscle is superior to that from the subcutaneous tissue. Clinically it was established in a limited number of cases of syphilis that salvarsan injected into this muscle excites a fairly rapid, unmistakably beneficial influence upon secondary and tertiary manifestations of syphilis and upon the Wassermann reaction without causing pain and other ill effects deserving any serious consideration. Meltzer gives the technique of these intramuscular injections in detail.

The External Application of Magnesium Sulphate in the Treatment of Erysipelas.—Choksy (*Lancet*, 1911, clxxx, 300) reports 72 cases of erysipelas treated by wet dressings of a saturated solution of magnesium sulphate in water as originally advocated by Lucker. Lucker has described this method of treatment in 19 cases of erysipelas complicated with alcoholism, acute nephritis, myocarditis, pneumonia, etc., with but three deaths, and in 35 uncomplicated cases without a single death. This treatment has been applied by him and others to nearly 700 cases of various forms of inflammation with uniformly good results, and Lucker claims the following advantages for it: (1) Magnesium sulphate is easily obtained, is inexpensive, non-toxic, and is easy of application. (2) The patient promptly obtains relief from the distressing local symptoms. (3) The temperature rapidly falls to normal, usually during the second twenty-four hours, thus eliminating possible complications from a more prolonged fever. (4) There is no necessity for internal medication in uncomplicated cases, the only treatment being a milk diet until the temperature becomes normal. Choksy found in his series of cases, that in almost every instance the immediate effects of the application of magnesium sulphate solution were extremely beneficial. Pain and swelling abated, fever decreased, and extension of the infection was controlled in all but 6 cases. Many of the cases were advanced and neglected, and consequently the results have not been so uniformly good as those reported by Lucker. In 6 cases the inflammatory process extended so rapidly that in spite of this treatment antistrepto-

coccus serum was injected; only 1 of these cases recovered. Excluding the above and 7 moribund cases, there remained 59 cases, with 13 deaths and 46 recoveries. equivalent to about 22 per cent. as compared with about 16 per cent. in Lucker's complicated cases.

The Treatment of Pernicious Anemia with Salvarsan.—Bromwell (*Brit. Med. Jour.*, 1911, 2619, 547) reports 2 cases of pernicious anemia treated with salvarsan. The first case received one injection of 0.2 gram and three injections of 0.3 gram. The hemoglobin rose from 50 per cent. to 78 per cent., and the red blood cells increased from 1,720,000 to 3,580,000. The second case received four injections of 0.3 gram of salvarsan and there was an increase of hemoglobin from 52 per cent. to 80 per cent., with an increase of the red blood cells from 1,760,000 to 4,020,000.

Adalin, a New Hypnotic.—Froehlich (*Berl. klin. Woch.*, 1911, xlviii, 18) has employed adalin, a new sedative and hypnotic in a large number of cases and says that its action is prompt, safe, and lasting. Adalin is a combination of bromine with diethyl-acetyl-urea and may be obtained in powder or tablet form. He used it in doses of 1 gram; if a second dose was necessary, 0.5 gram was given. It is best given with some warm drink. Froehlich noticed no cumulative action from its use, and there seemed to be no tendency for the drug to lose its effect when taken over long periods of time. He gives the details of the cases in which he used it, and found that it induced sleep when other hypnotics had failed.

Serum Treatment of Hemophilia.—Weil (*Rev. Française de Méd. et de Chir.*, 1911, viii, 23) reports several successful cases of the serum treatment of hemophilia. One patient suffered from severe attacks of spontaneous bleeding since infancy, at intervals of not more than three months. Treatment was started during an attack of hematuria, and since that time the patient has had no further attack of spontaneous bleeding. In the first stage of the treatment excessive hemorrhage following cuts did not occur, but recurred whenever the intervals of injection were lengthened. Four years later the patient suffered at intervals from some articular pains, but otherwise was reasonably well. The blood which formerly required four and one-half hours to coagulate now does so in forty to fifty minutes. A member of the same family suffered from the same condition and under treatment showed a similar improvement. Weil also mentions the case of a child, aged seven years, who was very much benefited. The cessation of bleeding in children was followed by a rapid increase in weight. The cases treated by this method are of course as liable to the danger of anaphylaxis as are any others continuously treated by serum therapy. Walters and Eaton used horse serum and antidiphtheritic serum in doses of 20 c.c., given subcutaneously and repeated the injections every two months.

PEDIATRICS

UNDER THE CHARGE OF

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Total Congenital Absence of the Teeth.—Wieting (*Deut. med. Woch.*, 1911, xxxvii, 504) reports the total absence of the teeth in a boy, aged twelve years, with slightly retarded physical development. The condition was congenital. The lips and orbicularis oris muscles were hypertrophied and the food was macerated mostly by the tongue. There was entire absence of the alveolar process and the matrix for tooth development. This was verified by the *x*-rays. There was no other abnormality of the body, nor of the hair or nails. But few similar cases are recorded in literature. Partch has reported several cases in which there was an absence of teeth on one side, and a corresponding absence of hair on the same side of the head. In this case Wieting could find no abnormality in any other respect, and there was no evidence of cretinism, syphilis, or rickets to throw any light on the etiology of the case.

Chronic Lung Affections in Children.—Sawyer (*Brit. Jour. Child. Dis.*, 1911, viii, 151) describes the chronic lung affections in children under two heads—bronchial catarrh and a mild form of bronchiectasis. These chronic conditions are difficult to diagnosticate owing to an absence of abnormal physical signs. In cases of chronic bronchial catarrh the children may have a cough for many years, with scarcely any abnormal physical signs. They are usually delicate and anemic, but show no signs of cyanosis. There is no clubbing of the fingers or dyspnea, but there is a tendency to have many colds. The cough has existed from infancy in many cases, or from some former febrile attack. Expectoration is usually absent. A few rhonchi are heard at times when the patient has a cold, but no coarse lesions are demonstrable. In establishing a diagnosis the most important part of the history is the duration of a cough for several years; this rules out tuberculosis. Recovery often occurs with the growth of the child. Enlarged tonsils, adenoids, and neuroses must be excluded in making the diagnosis. Chronic bronchitis in infants is rare. It is, however, constant in scoliosis. In chronic bronchitis the patients resemble the first group alluded to, but usually have cyanosis, more frequent cough occurring in paroxysms, and usually some phlegm. Rhonchi and coarse rales are present in the lungs, which show signs of emphysema. The physical signs in the lungs are bilateral, and there is no wasting or fever. The treatment is similar to that prescribed in adults, and most benefit is derived from potassium iodide. Bronchiectasis in a mild form is found quite often, but severe types are rare. As the child grows older the bronchi often resume their normal size. Here there is a constant cough and a large quantity of phlegm with a slightly fetid smell. There

is usually slight clubbing of the fingers, but not much wasting or nocturnal fever. A few rhonchi are usually heard at the bases. There is no consolidation, as a rule, and the breath sounds and percussion note are normal. The rare, severe forms show moderate wasting, fever, cyanosis, a large amount of phlegm, and definite clubbing of the fingers. There may be contraction of one side of the chest with displacement of the heart toward that side and emphysema of the opposite lung. There may be septic cachexia. The treatment, besides general hygiene, consists of continual inhalation of drugs on a "Yeo" inhaler. Four drops of a mixture of creosote, ʒij; carbolic acid, ʒij; tinct. iodine, ʒj; spiritus etheris, ʒij; and spiritus chloroformi, ʒij, are placed on the sponge every two hours during the day, and three times at night. Phthisis of the adult type is very rare in children under fifteen years.

Ephemeral, Traumatic Glycosuria in the Newborn.—Erich Hoeniger (*Deut. med. Woch.*, 1911, xxxvii, 500) reports 4 cases of transient glycosuria in newborn infants delivered with forceps. In all the cases the family history of the mother showed no diabetes. Sugar was present in the urine of the four infants up to the second, third, and fourth day after birth, when it disappeared. The deduction follows that the sudden trauma of the forceps on the child's head is the cause of the glycosuria, since normally born children, even where the labor is very difficult and the head subject to much pressure, do not show any signs of glycosuria. These cases are reported to encourage investigation along this line, especially to determine whether these temporary glycosurias may be the beginning of a diabetes mellitus later on in childhood.

Petechial Hemorrhages from Artificial Stasis as a Diagnostic Help in Scarlet Fever.—Leede (*Münch. med. Woch.*, 1911, lviii, 293) describes a diagnostic point in scarlet fever. During an epidemic, while taking blood from veins in the arm of scarlet fever patients, he noticed that soon after compressing the arm with a bandage hemorrhages appeared in the skin distally from the bandage. These petechiæ always appeared in those suffering from scarlet fever, but did not seem to occur in those suffering from other diseases. A study was made of this phenomenon, using a rubber tourniquet on the upper arm sufficiently tight to cause venous stasis, but not compressing the arterial flow. Almost without exception in several hundred cases of scarlet fever tested, more or less extensive hemorrhage appeared under the skin. Control tests in conditions other than scarlet fever showed occasional slight tendency to similar petechiæ, although this was far from constant. Even in healthy individuals this reaction was noted in a very few cases. It was determined that the grade of the reaction depended on the resistance of the capillaries, which in scarlet fever is much impaired by the toxins of the disease. To determine this grade of reaction a modified Riva Rocci blood pressure apparatus was used. The systolic and diastolic pressures were determined. The cuff was then filled with air until a pressure was reached just below the diastolic pressure, usually 45 to 60 mm. of mercury. This pressure was maintained for from five to twenty minutes, and the skin watched for petechiæ, which develop in from five to twenty minutes, usually at the

bend of the elbow. In this way the veins are blocked and the arteries are not compressed, and the stasis is developed from *vis a tergo*. In other conditions it was exceptional to get a result similar to this; only in measles were results noted which at all approached those found in scarlet fever. This phenomenon appears fairly early in the disease, at least with, and occasionally before, the appearance of the eruption. The capillary susceptibility diminishes as convalescence goes on, and while the majority showed the phenomenon up to the forty-second day, in a large number of cases the reaction could not be elicited after the twenty-first day of the disease. Females seem to lose the reaction earlier than males. Only in one clinically typical case of scarlet fever did this reaction fail, and this was probably due to subcutaneous fat. To make this test place a rubber bandage around the upper arm, causing venous distention, but not occluding the arterial pulse. In from five to fifteen minutes the bandage is loosened. The tender skin at the angle of the elbow is then put on the stretch to determine a sprinkling of dark petechial hemorrhages.

Confirmation of Rumpel and Leede's Phenomenon in Scarlet Fever.—Bennecke (*Münch. med. Woch.*, 1911, lviii, 740) confirms the findings of Rumpel and Leede in regard to petechial hemorrhages from artificial stasis in scarlet fever. He has noticed this phenomenon frequently in making blood examinations in scarlet fever, and found it positive in 26 out of a series of 32 cases. In doubtful cases in children, where the throat signs were suspicious, a positive result was always confirmed by the development of typical scarlet fever. He found the result positive in 1 case of measles and in 2 cases of high arterial tension (230 mm.), in which latter cases, however, the spots spread over the forearm and hand and remained visible from two to three weeks. The typical lesions were found only about the elbow, the small, pinhead-sized hemorrhages disappeared quickly, the larger sized petechiæ disappearing in from one to two days. In the two cases of high arterial tension the petechiæ became pigmented. The negative result of this test speaks against scarlet fever. The positive result does not absolutely prove scarlet fever.

Edema during Gastro-intestinal Conditions in Infants.—Hugh Ashby (*Practitioner*, 1911, lxxxvi, 686) calls attention to the edema of the feet and hands which often develops during a gastro-intestinal disease in infants. The edema usually appears toward the end of an attack of gastro-intestinal catarrh, when the vomiting and diarrhea are getting better. It does not develop during the acute stage. The edema is bilateral and attacks the dorsum of the hands and feet, and occasionally the face becomes puffy, giving the appearance of a renal condition. The heart and lungs are usually found normal. The urine is high-colored, acid, and foul-smelling, and contains a few leukocytes, but no blood or casts. Small amounts of albumin are found at times, but while there is no nephritis, there is renal inadequacy and the child is suffering from toxemia. Necropsy shows no change in the kidneys, except slight cloudy swelling in the tubules. The blood in these cases shows a high proportion of hemoglobin and a slight increase in the number of red blood cells. The circulation is not especially feeble.

Edema in the course of gastro-intestinal diseases is a serious symptom, although quite a large number of cases recover. The chlorides are not diminished in the urine, as they are in cardiac diseases with edema. In the treatment of this condition, besides general hygienic measures, it is important in feeding to exhibit a high percentage of proteid and a low percentage of fat and carbohydrate. Potassium citrate is the best diuretic. Tincture of digitalis in $\frac{1}{10}$ drop doses every two hours for a short time is often of service.

OBSTETRICS

UNDER THE CHARGE OF

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Our Recent Advances in Obstetric Surgery of Proved Value.—Those who enjoy a critical review of modern methods will find much of interest in a paper by Roth, read before the Gynecological Society of Dresden (*Zentralbl. f. Gynäk.*, 1911, No. 7). He reviews the literature recently published, advocating the early getting up of puerperal patients. Krönig has enthusiastically advised the early rising of puerperal patients, even in cases which ordinarily would seem to demand especial caution. For this practice he claims a reduction of mortality to 4.3 per cent., and in 1000 patients no case of thrombosis. The other side of the picture is presented by Frommé, who allowed a primipara, aged nineteen years, to get up for one hour on the second day of the puerperal period. This was followed by fever lasting for four days, and the development of embolism, which ended the patient's life on the eleventh day. Roth believes that we should not abandon the custom of keeping puerperal patients in bed from seven to eight days. He finds no adequate reason for changing this practice. The treatment of placenta prævia by section is also reviewed, and the comparative mortality of section and other methods of treatment is stated. By non-surgical methods, a maternal mortality of 6.6 per cent. is reported, and a fetal mortality of 30 per cent. Roth would agree with Veit in declining to adopt Cesarean section for placenta prævia on the ground that no better results will be obtained than follow other methods of treatment. The suprasymphyseal section receives also an adverse verdict, and the statement is made that in two years after its enthusiastic introduction it has made no essential headway. The field for vaginal section is thought to be an exceedingly limited one. It is always beneficial to consider critically any method of operation which is an essential change from methods which have been proved to be of value. In the treatment of placenta prævia by section, the critic does not distinguish between central placenta prævia and other varieties. In partial, marginal, and lateral placenta prævia the rupture of the membranes and the stimulation

of uterine contraction is sufficient in many cases. In others, the introduction of a bag through the ruptured membranes, and through a portion of the placental substance, has been proved to be of value, but in complete placenta prævia, with mother and child in good condition, the classic Cesarean section, when promptly done in the hospital, gives results superior to other methods of treatment.

Spontaneous Gangrene in both Ischiorectal Fossæ.—Leyzerowicz (*Zentralbl. f. Gynäk.*, 1911, No. 8) reports the case of a woman, aged twenty-two years, who gave birth at full term to a living child in spontaneous labor, with normal expulsion of the placenta and without laceration. On the seventh day of the puerperal period the patient's temperature rose to 104°. She had no abdominal pain, but complained of severe pain in the region of the sacrum. The lochial discharge was normal, and the bowel movement normal. The uterus was twice curetted without result. Later, redness developed in the region of the anus, and preparations were made to practise incision and drainage. The swelling opened spontaneously, and purulent fluid escaped. The opening was dilated, and necrotic material and decomposed fluid escaped. A considerable portion of tissue had become gangrenous. A second opening in the other ischiorectal fossa developed, which was similarly treated. The patient made a tedious recovery.

The Repair of Vesical Vaginal Fistula after Hebostiotomy.—Christofoletti (*Zentralbl. f. Gynäk.*, 1911, No. 8) reports the case of a patient who had a very small fistula communicating with the neck of the bladder near the urethra. Two operations were performed to close this fistula, but unsuccessfully, and pregnancy supervened, which was terminated by Cesarean section. Eight weeks after operation the fistula was closed by separating the bladder from the pubic bone and bringing together the edges of the fistula with two rows of catgut stitches. From this time the patient made a good recovery. He also reports the case of a patient who four years previously had hebostiotomy performed, the puerperal period being complicated by fever. There was no laceration of the vagina, but the patient did not retain the urine. Operation was performed, as in the first case, by loosening the bladder from the pubic region and bringing the edges together in layers. A good result followed.

Myoma Complicating Pregnancy.—Schauta (*Zentralbl. f. Gynäk.*, 1911, No. 8) reports the case of a patient, six months pregnant, who suffered from pain in the left side of the abdomen. This became so severe that the patient willingly consented to operation. A tumor as large as a kidney was found upon the left side of the pregnant uterus. Incision was made along the border of the left rectus muscle and a myomatous tumor found attached to the uterus by a broad pedicle. The tumor was removed and the tissues brought together. Pregnancy proceeded without interruption. On examining the tumor it was found to be a necrotic myoma. The necrotic process evidently had something to do with the patient's pain. In discussion, Fabricius, in 578 operations for myoma, had 9 cases complicated with pregnancy, 1 of these having an ovarian cyst in addition. In 223 cases, 5 opera-

tions upon myomatous tumors were performed because of pregnancy as a complication. These cases were treated by supravaginal amputation of the uterus. He also reports the interesting case of a patient, aged thirty years, who at the fourth month of pregnancy had the uterus increase so rapidly that at six months it filled the entire abdomen. Abortion occurred, with the expulsion of the fetus, and upon examination a soft tumor as large as the head of a child was found in the right wall of the uterus. The placenta had been partially attached to this tumor. The tumor steadily decreased in size, and eight days after the abortion could scarcely be detected. A subsequent pregnancy occurred which proceeded normally, with normal labor. At this time scarcely a trace of the tumor could be found. A second case is also reported in which the tumor grew very much less after the birth of the child. Peham, in 117 cases, had 8 complicated by pregnancy. Two were treated by conservative methods, removing the tumor without interrupting the pregnancy. In one case the tumor was so large that operation was necessary.

Advanced Extra-uterine Pregnancy.—Wagner (*Zentralbl. f. Gynäk.*, 1911, No. 8) reports the case of a patient who came to his clinic in a pregnant condition complaining of almost constant pain in the abdomen. When pregnant about six months the fetal movements ceased, and the abdominal pain grew very much less. On examination, the abdominal tumor extended two fingers beneath the tip of the sternum. The head of a full term fetus could be palpated in the abdomen, and the pelvic tissues showed signs of pregnancy. The placenta could be made out as a comparatively soft mass attached to the uterus by a pedicle. Operation was performed under lumbar anesthesia and the tumor was covered by the omentum which was adherent to the pelvic brim. After this was loosened the fetus was found in a grayish-white capsule. The tumor, which was supposed to be the placenta, was a hydrosalpinx as large as an orange. On the right side the tube terminated in a grayish-white hard tumor as large as two fists, which was attached to the sac containing the fetus. This tumor was adherent to the surrounding tissues. The appendix was adherent to a smaller tumor. The ovaries were normal, and the uterus and left ovary were left. The hydrosalpinx, fetus, and placenta were removed. On examination, it was found that the fetus had now become a lithopedion. The placenta showed calcareous changes, and was contained in a sac composed of the tube. The fetal sac was connective tissue developed in a plastic peritonitis, and the sac was so adherent to the fetus that some of the hair from the scalp was firmly fixed in the sac. There was no amniotic liquid. The left foot of the fetus was much bent, but otherwise the skeleton was normal. There had been no symptoms of intraperitoneal hemorrhage or acute peritonitis.

Momburg's Method for Controlling the Circulation in the Pelvis.—Momburg (*Archiv f. klin. Chir.*, 1911, Band lxxxix, No. 4) again draws attention to the value of his method in preventing pelvic hemorrhage. In 17 obstetric cases he was able to render the uterus practically anemic and bring about vigorous uterine contraction. He

uses from two to four bandages, and, in addition to that passed about the abdomen, he bandages the lower extremities also. Anesthesia may be used, and it is found that less ether than ordinarily is required. The patients recover speedily after anesthesia. The heart action is sometimes weaker than normal and requires stimulation, while in other cases its function is undisturbed. In cases coming to section no injury to the abdominal viscera has been found. The bandages can remain, if necessary, for two hours. If anesthesia is not employed morphine should be given.

GYNECOLOGY

UNDER THE CHARGE OF

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Sacro-iliac Relaxation.—Meisenbach (*Surg., Gyn., and Obstet.*, 1911, xii, 411) draws attention to the fact that the sacro-iliac joint is, contrary to the older teaching, a true joint, possessing a hyaline articular cartilage, a synovial membrane, capsule, and ligaments, and that it normally permits of a slight degree of motion, varying in individual cases. When the pelvic ligaments have a normal tonus the joint can withstand considerable strain, but when they become relaxed, the joint yields easily, and may cause many marked symptoms ordinarily referred to intrapelvic conditions, but which are not relieved by the gynecological operation which appears to be indicated. Among several causes, however, which may produce a relaxation of the sacro-iliac ligaments, Meisenbach considers pelvic congestion as one of the most important; the condition also often arises after childbirth, especially after a high forceps delivery. Many of these cases receive no relief from gynecological treatment, but if properly diagnosticated and treated they can almost always be rescued from chronic invalidism. Meisenbach considers stereoscopic *x*-ray pictures of considerable value in diagnosticating a sacro-iliac relaxation, whereas in the ordinary plate it usually passes unnoticed. The treatment is a properly applied plaster or celluloid jacket, steel braces, elastic webbing, etc., according to individual indications. Strapping by means of adhesive strips applied firmly from one crest to the other may afford temporary, but only temporary, relief.

Treatment of Cystocele.—Brenner (*Monats. f. Geburts. u. Gyn.*, 1911, xxxiii, 464) asserts that the only really fixed portion of the bladder is that directly over the anterior cervical wall, and that this is the first part of the bladder to enter into the formation of a cystocele, which, therefore, can only occur when the union between the bladder and the anterior cervical wall has given way. Acting on this anatomical

principle, he suggests the following operation for the treatment of the condition. The bladder wall is exposed through the vagina, and its most prominent portion folded in by two purse-string sutures after Gersuny. A posterior colporrhaphy and perineorrhaphy are performed in the usual manner. The abdomen is then opened by a transverse fascial incision, the peritoneum of the anterior surface of the uterus incised from one ligamentum teres to the other and dissected downward till the turned-in bladder diverticulum and the vaginal wall come into view. The infra-ureteral bladder tissue is now puckered together with one or two sutures, after having previously dissected out bluntly the vesical ends of the ureters, great care being taken in introducing these sutures in no wise to disturb the course of the ureter. In this way a firm point of resistance is secured below the ureters and the midsection of the bladder and above the vaginal vault. Then by means of a transversely placed suture the posterior wall of the bladder is fastened to the anterior wall of the cervix; a second similar stitch is placed somewhat higher up nearer to the fundus of the bladder. The peritoneum is then closed, the uterus suspended to the anterior abdominal wall if necessary, and the wound closed. The author maintains that the result obtained by this infra-ureteral suture cannot be attained from below, as the ureters cannot be dissected out without injuring their attachments, and without dissecting them out there is too much danger of including them in the suture, or, at least, of kinking or injuring them. He considers that almost all of these cases have a retroverted uterus, which of itself calls for the performance of a laparotomy.

Relation of the Thyroid to the Ovaries.—Goodall and Conn (*Surg., Gyn., and Obstet.*, 1911, xii, 457) report an interesting case of a markedly enlarged thyroid in a woman, aged sixty years, associated with chronic pelvic tuberculosis, in which the thyroid swelling completely disappeared after removal of the diseased pelvic organs, and then proceed to discuss in detail the relations between the thyroid and the female genital organs, considering this subject from the point of view (1) of the influence of the thyroid upon the genital system, and (2) of the influence of sexual function upon thyroid activity. Under the first heading a group of cases is quoted from Goodall and Conn's experience in which myxedema or other symptoms of a diminished thyroid were associated with diminished or absent menstrual function. In some of these cases most distressing menstrual molimina, going as far as epileptic attacks, occurred at the time when menstruation should have taken place. In all of these cases a marked improvement followed treatment with thyroid extract, in some instances combined with calcium lactate. To illustrate the influence of hyperthyroidism on the sexual function several caess are quoted from Pinard, in which marked menstrual disturbances, usually of the amenorrheic type, were associated with exophthalmic goitre. In discussing the influence of the sexual function upon thyroid activity, Goodall and Conn call attention to the relief of the symptoms often following a natural or artificial menopause, supposed to be due to a loss of balance between the ductless glands produced by small doses of thryoid extract. An overproduction of the ovarian secretion, on the other hand, seems to

cause hyperactivity of the thyroid gland, so that these two glands are to be considered as neutralizers, not as compensators, of each other. This idea is further borne out by the fact that an enlargement of the thyroid gland takes place at puberty, and frequently at the onset of pregnancy, at both of which times a physiological increase in the internal secretion of the ovary occurs. Goodall and Conn emphasize the fact that the action of any two of the ductless glands should not be considered alone, as all these glands are most intimately associated in function. They consider that the facts already brought out—also that exophthalmic goitre almost invariably makes itself manifest during the years of greatest sexual activity, whereas myxedema and cretinism generally occur before or after sexual life—lend weight to the supposition that the thyroid and ovarian glands are under the control of the same governing centre, or that they depress and stimulate each other into activity.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES

UNDER THE CHARGE OF

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Vincent's Angina Involving the Larynx Exclusively.—Arrowsmith (*Annals of Otology*, September, 1910) reports this case in a stableman, aged twenty-six and one-half years, admitted to hospital with œdematous epiglottis, arytenoids, and ventricular bands, the dyspnœa which became so urgent as to compel hurried tracheotomy twenty-four hours later. The tube was removed after four days and the suppurating tracheotomy wound was completely healed by the third week. Resuppuration ensued, with a recurrence of hoarseness, dyspnœa, and swelling of the soft tissues of the neck, so that a second tracheotomy became necessary. In less than a month this had to be followed by a thyrotomy and the insertion of a laryngostomy tube for the purpose of keeping the larynx open. At the time of the report the patient was unable to breathe at all adequately upon closure of the tracheal orifice. Arrowsmith also reports a more recent case in a male, aged forty-one years, the exudate from whose throat showed numerous fusiform bacilli and spirilla of Vincent implanted upon a tuberculous larynx.

Diverticulum of the Trachea.—Kahler (*Annales des maladies de l'oreille, du larynx, du nez et du pharynx*, August, 1910) has reported a case of diverticulum of the trachea, discovered accidentally, in a man, aged thirty-four years, who was being treated for spasm of the esophagus at Chiari's clinic.

Intralaryngeal Actinomycosis.—Arrowsmith (*Laryngoscope*, October, 1910) describes a case of apparently primary intralaryngeal actinomycosis in a male subject, aged nineteen years. Specimens removed from the mass after careful examination allowed no other diagnosis than that of actinomycosis, but a month later no evidence of actinomycosis could be found in the sputum, while tubercle bacilli, staphylococci, and streptococci were present. The case progressed as one of tuberculosis of the larynx.

Laryngostomy in Perichondritis of the Larynx.—Yvanov (*Annales des maladies de l'oreille, du larynx, du nez et du pharynx*, August, 1910) reports that he has treated the losses of substance of the anterior wall of the trachea in eight instances by the procedure of Mangoldt; but in one case he used successfully the cartilage of the nasal septum in place of costal cartilage. In four of these patients respiration by the normal passages had been completely reëstablished, but the others were still under treatment.

Paralysis of the Recurrent Laryngeal Nerve.—Mead (*Jour. Amer. Med. Assoc.*, December 24, 1910) reports a case of persistent patency of the ductus arteriosus in which there was fixation of the left vocal band in the median line from pressure on the abductor fibers of the recurrent laryngeal nerve. In a discussion upon this case, Tileston mentioned that von Schroetter, Jr., of Vienna, reported a similar case a few years ago, at that time the only one to be found in literature.

New Oral Speculum for Direct Examination of the Mouths of the Eustachian Tubes and Parts Adjacent.—Yankauer (*Laryngoscope*, March, 1911) describes and depicts an ingeniously devised speculum which exposes the pharyngeal extremities of the Eustachian tubes and the fossa of Rosenmueller, by direct inspection. With its aid adenoid masses can be seen, and be removed with the straight forceps. The interior of the fossa can be seen, probed, irrigated, and packed. Adhesions can be cut with straight scissors and applications made with an ordinary applicator. A small tube about one-fourth inch in diameter can be introduced into the interior of the Eustachian tube, and its lumen examined down to the isthmus.

Auto-inspection of the Vocal Apparatus during Phonation.—Wright (*Laryngoscope*, March, 1911) describes and depicts a modification of Hays' pharyngoscope with an angular telescopic extension reaching to the eye, by which a person may see with wonderful clearness the operation of his own vocal apparatus while producing sound.

Grave Hemorrhage after Tonsillectomy.—Marschik (*Revue Hebd. de lar., d'otol., et de rhinol.*, April 15, 1911) reports a case in which it became necessary to suture the pillars of one side upon a tampon of iodoform gauze, and to tie the external carotid on the other side and follow that by an infusion of adrenalinized physiological serum. The patient recovered. The hemorrhage was attributed to the facts that the patient had nephritis, was in the second day of her menstruation, and had been very indocile under the operation.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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Experimental Contribution to the Study of Cardiac Hypertrophy.—Hugh A. Stewart (*Jour. Exp. Med.*, 1911, xiii, 187) has studied the hypertrophy of the heart of dogs following upon the production of an aortic insufficiency. The aortic insufficiency was made by means of the valvulotone described by McCallum. Following the lesion at intervals varying from five to one hundred and twenty days, the animals were killed and their hearts weighed by the Müller method. Not only was the proportional weight of the whole heart estimated, but that of the auricles, ventricles, and the septum separately. The experiments showed that hypertrophy starts very shortly after the production of the aortic insufficiency, and is well marked at the end of a week, and that all chambers of the heart shared in the increase of weight of the heart. The greatest absolute increase, however, is in the left ventricle. The greatest relative increase is also in the left ventricle, but the auricles show a relative hypertrophy greater than that of the septum or of the right ventricle. This hypertrophy of the right auricle with experimental aortic insufficiency has been noted by others, notably Rosenbach and Senator. The simplest explanation is that the hypertrophy depends upon a relative mitral insufficiency which is so commonly associated in man with aortic insufficiency. The presence of a relative mitral leak could, however, not be established in these experiments, and the explanation seems to depend upon other factors. There is no altered venous pressure in the auricle, but there is a marked increase in the force of the auricular systole, which probably explains the co-hypertrophy of the auricles. During the first week after the production of the aortic insufficiency there is only a very small increase in water content of the heart, and consequently it is not possible that the rapid increase in weight during this time could be due entirely to increased water content of the muscle fibers.

The Passage of Antitoxic Sera into the Cerebrospinal Fluid.—It has been known for some time that crystalloids when injected subcutaneously pass with great difficulty or not at all into the cerebrospinal fluid, and it is probable that the same is true of colloids. Lemaire and Debre (*Jour. de Physiol. et de Path. Gén.*, 1911, xiii, 233) have made some experiments to test the accuracy of this last statement and to determine, as well, whether the protective property of immune sera injected subcutaneously is demonstrable in the spinal fluid. Dogs were injected subcutaneously with tetanus antitoxin from the horse and the cerebrospinal fluid examined later by the precipitin reaction to see whether it contained horse serum, and by injections into animals to determine whether it had acquired the property of protecting these

animals against tetanus toxin. It was found that only infinitesimal amounts of horse serum passed into the spinal fluid, and that the fluid had acquired very slight protective power against tetanus toxin. The blood serum of the dogs, however, contained large quantities of horse serum albumin and developed marked antitoxic qualities. Experiments were then instituted to see if by any means the foreign serum could be made to pass more readily into the spinal fluid. Morphine was administered to the dogs in doses of one centigram per kilo. Under these circumstances, though the amount of horse serum was not perceptibly increased in the spinal fluid, the antitoxic power was very distinctly increased. At the same time the antitoxic power of the blood serum was reduced. They believe that this is to be accounted for by the dilating action of morphine upon the peripheral vessels. They believe that this action of morphine in lowering the antitoxic effect of the blood serum after subcutaneous injection should be borne in mind when sera are administered to man for therapeutic purposes.

The Value of the Treatment of Acute Articular Rheumatism with the Antipyretics.—Menzer (*Zeit. f. Hyg. und Infektionsk.*, 1911, lxviii, 296) brings up the oft discussed question as to the value of the salicylates in the treatment of rheumatic fever. He believes that the disease is a streptococcus infection originating in the tonsils and upper air passages and thence becoming generalized. The inflammatory processes which arise during the course of the disease, in the joints, heart, and serous membranes are manifestations of an attempt upon the part of the body to combat the local infection in these situations and therefore represent the first efforts at healing. Such local reactions cannot be prevented by any method of treatment, and the question at issue is by what method can complete recovery best be brought about. He uses large statistics gathered from the army to show that treatment by the salicylates does not in the long run further the healing process, inasmuch as the cases treated with antipyretics showed a larger percentage of serious injuries to the heart and a greater number of recurrences. He suggests that the salicylates should be replaced by local and general methods such as are usually in vogue for the alleviation of general and localized infections. Such procedures as warm applications, baths, and general attention to the nutrition of the patient might be supplemented by injection of small doses of antistreptococcus serum.

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ORIGINAL ARTICLES

SO-CALLED LARVAL HYPERACIDITY.[1]

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It is a well-known fact that certain patients present symptoms which are manifestly those associated with hyperchlorhydria, and yet on examination of the gastric contents not only do not present an increase in free hydrochloric acid, but often hypochlorhydria or even complete anacidity is revealed. This finding has been accounted for in various ways, but it is generally believed that there is frequently a state of gastric hyperesthesia at hand in which the gastric mucosa is so sensitive that it does not tolerate even normal or lessened amounts of acid. This condition is occasionally found in achylia gastrica, in which symptoms of hyperacidity may exist, with an entire absence of hydrochloric acid. Aside from these cases, however, there are a certain number manifesting similar symptoms, in which the gastric contents reveals a normal percentage of acid or even subacidity, and yet present in the earlier stages of digestion a most marked hyperchlorhydria.

Straus[2] was the first to point out the fact that symptoms of hyperacidity may exist without an actual increase in hydrochloric acid, and Roth and Straus[3] explain this state by assuming that there is an actual hyperacidity which is not revealed, because the exam-

[1] Presented at the annual meeting of the American Gastroenterological Association, held in Philadelphia, April 20, 1911.

[2] Deut. Archiv f. klin. Med., 1896, Band lvi, S. 120.

[3] Zeitschrift f. klin. Med., Band xlvii.

ination of the gastric contents is made an hour after the test breakfast is given, and that two elements exist in the formation of the gastric secretion—an inactive diluting fluid and an active form whose specific action is to digest proteids. The active digestive secretion is gradually diluted by the diluting fluid. It is, therefore, easily conceived how, if the diluting fluid be secreted rapidly, a gastric juice which is hyperacid when first secreted (secretio celer et magno) may be rapidly reduced to normal or subnormal.

Schüler[4] carefully investigated this condition further, and presented seventeen cases in which the gastric contents showed similar characteristics presenting the clinical picture of a hyperacidity, and yet having a normal percentage of free hydrochloric acid. He termed this condition "hyperaciditas larvata" in contradistinction to the usual form known as a "hyperaciditas manifesta."

In the larval form there is probably, as Schüler points out, an actual hyperacidity, which is, however, not revealed, inasmuch as the gastric contents are usually extracted an hour after the test breakfast has been given. It is probable that the secretion, which at an earlier period of digestion might appear hyperacid, is gradually neutralized, so that at the end of an hour it will present a normal or diminished amount of acid. Schüler termed this condition "secretio alta et celer."

My own observations with this condition extend over a series of six cases. Of these, there are 4 males and 2 females. The ages vary between twenty-six and fifty-eight years. The symptoms are largely those of a neurasthenia, evincing at the same time special manifestations of hyperchlorhydria, consisting of pain and pressure in the region of the stomach one hour after meals, and extending over a period of from one to one and one-half hours, and usually relieved at the end of this time, or at any time, by the ingestion of food. Of the other symptoms noted, acid eructations, heartburn, nausea, and occasionally vomiting of acid material are most prominent. The appetite is usually increased, though on account of the pain induced by the ingestion of food there is usually fear of eating. In not one of our cases could an epigastric painful area be detected, and occult blood was always absent in both gastric contents and in the stools. In all instances general nervous symptoms were manifested, as headaches, insomnia, lassitude, irritability, and depression, with periods of discomfort alternating with accountable periods of well-being, the periods of discomfort often being induced by nervous influences, such as shock or anxiety. The quantity of gastric contents obtained is always large, varying between 215 and 368 c.c., always a most significant feature of this condition. The appearance of the contents is also characteristic, consisting largely of a watery secretion containing but little sediment. On standing,

[4] Deut. med. Woch., 1900, S, 303.

two layers are formed—a lower, slight in amount, but with solid sediment, and above a clear layer, larger in quantity. After centrifugalization the amount of solid sediment in proportion to the total sediment is constantly under 22 per cent., while the fluid contents ranges as high as 90 per cent. Under normal conditions the amount of the solid sediment is as 40 is to 60 to the total sediment; the variation from the normal is an additional evidence, therefore, of the presence of a larval hyperacidity. The specific gravity of the gastric secretion varies between 1010 and 1014, reduced from the normal of between 1015 and 1020. The total acidity as well as the percentage of free hydrochloric acid is always normal, the former varying between 38 and 56, the latter between 30 and 44, though in the earlier period of digestion a high total acidity as well as a marked hyperchlorhydria is always manifested. The amidulin reaction is present in all instances. Numerous examinations were made upon all the patients. The results of these examinations, after taking an Ewald test breakfast, are embodied in the following table:

No.	Name.	Sex.	Age.	Quantity of contents obtained in cubic centimeters.	Specific gravity.	Total acidity.	Free HCl.	Remains. Percentage.		Amylolysis.
								Solid.	Fluid.	
1	F. R.	M.	26	280	1012	44	32	22	78	Amidulin
				245	1014	42	36	16	84	Amidulin
				310	1013	48	38	18	82	Amidulin
				240	1015	40	32	10	90	Amidulin
2	L. K.	M.	39	334	1010	52	40	12	88	Amidulin
				306	1011	46	38	22	78	Amidulin
				250	1013	56	36	10	90	Amidulin
3	M. G.	M.	42	224	1014	48	42	18	92	Amidulin
				215	1014	44	40	20	80	Amidulin
				284	1010	42	34	14	86	Amidulin
				248	1012	50	44	18	82	Amidulin
4	S. H.	F.	37	312	1012	38	30	14	86	Amidulin
				340	1014	40	32	16	84	Amidulin
				368	1011	40	30	18	82	Amidulin
5	L. J.	M.	58	298	1012	54	38	18	82	Amidulin
				252	1014	56	34	14	86	Amidulin
				282	1010	54	38	16	84	Amidulin
				296	1011	50	36	20	80	Amidulin
6	P. M.	F.	46	340	1011	48	40	12	88	Amidulin
				325	1012	56	42	14	86	Amidulin
				336	1011	54	40	18	82	Amidulin

In order to study the state of the gastric secretion more carefully, the contents of the stomach was removed in all instances at intervals of fifteen, thirty, forty-five, sixty, seventy-five, and ninety minutes after the ingestion of an Ewald test breakfast, and at thirty, sixty,

ninety, one-hundred and fifty, one hundred and eighty, two hundred and ten, two hundred and forty, two hundred and seventy minutes after a Riegel test dinner. The results are embodied in the diagrams represented below. In order to more clearly portray the variations from the normal, diagrams of the digestion under normal

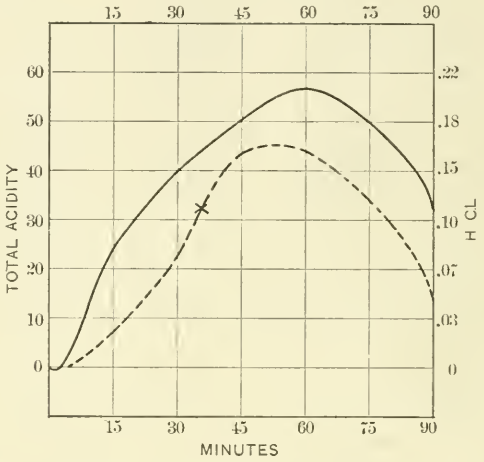

Diagram 1.—Curve of acidity in a normal case after an Ewald test breakfast. Solid line = total acidity; dotted line = HCl; × = free HCl.

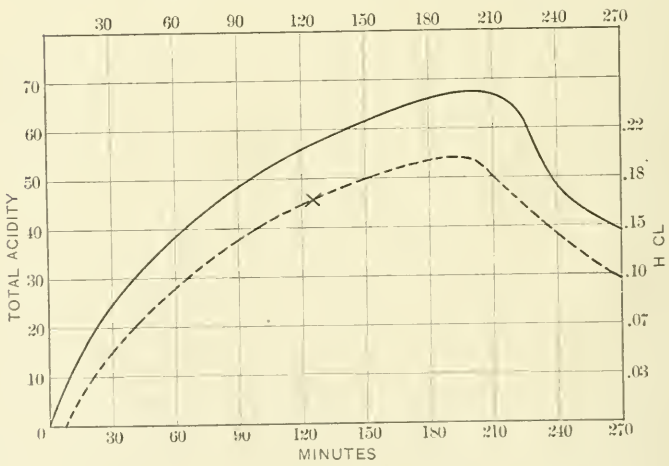

Diagram 2.—Curve of acidity in normal case after a Riegel test dinner. Solid line = total acidity; dotted line = HCl; × = free HCl.

condition, after an Ewald test breakfast and a Riegel test dinner, are also appended.

It may be readily observed that in place of the height of digestion appearing, as under normal condition, in from forty-five to sixty

minutes after an Ewald test breakfast, in cases of larval hyperacidity this condition presents itself, as regards the total acidity, in from twenty-eight to thirty-five minutes, and as to the free hydrochloric acid in from twenty-eight to thirty-three minutes.

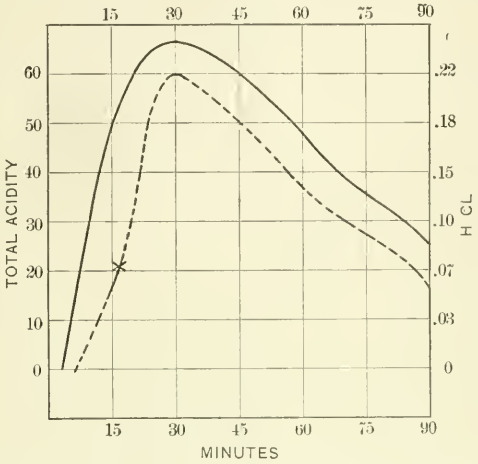

Diagram 3.—Curve of acidity in a case of larval hyperacidity after an Ewald test breakfast. Solid line = total acidity; dotted line = HCl; × = free HCl.

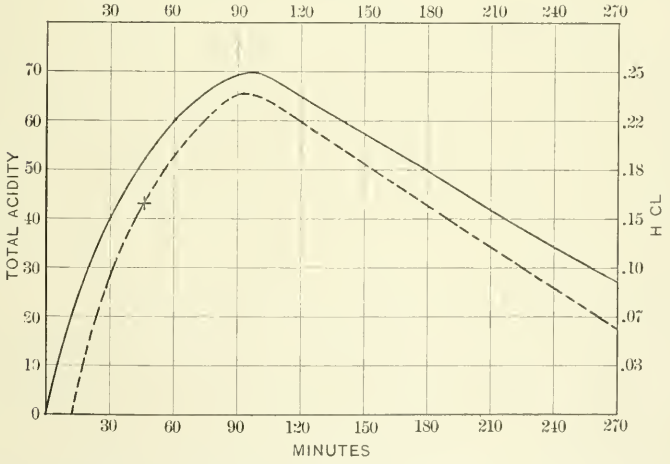

Diagram 4.—Curve of acidity in a case of larval hyperacidity after a Riegel test dinner Solid line = total acidity; dotted line = HCl; × = free HCl.

Under normal conditions, after a Riegel test dinner, the total acidity attains its height in from one hundred and eighty to two hundred and ten minutes, and the free hydrochloric acid in from one hundred and eighty to two hundred minutes. In larval hyperacidity this occurs much earlier, with the total acidity in from

eighty to one hundred and twenty minutes and with the free hydrochloric acid in from eighty to one hundred and ten minutes. The free hydrochloric acid, which under normal conditions first manifests itself in about thirty minutes after an Ewald test breakfast, and in about one hundred and thirty minutes after a Riegel test dinner, reveals itself in larval hyperacidity in from twenty to twenty-two minutes after an Ewald breakfast and in from thirty-six to forty-five minutes after a Riegel dinner. In larval hyperacidity the total acidity may reach 68 and the free hydrochloric acid 0.22 per cent., while in from forty-five to sixty minutes after a test breakfast or one hundred and eighty to two hundred and ten minutes after a test dinner the curve of the acidity has already fallen quite markedly. The diagnosis of larval hyperacidity does not usually present any difficulty. The symptoms of hyperacidity which arise early in the period of digestion, together with the characteristic features of the gastric contents, the large amount obtained consisting mainly of a watery secretion, with a low specific gravity, and with a normal acidity, and presenting the amidulin reaction distinguish this condition from the usual forms of hyperchlorhydria. The absence of an epigastric painful area, as well as the absence of occult blood in the stools, distinguishes it from gastric ulcer. Larval hyperacidity is differentiated from digestive or alimentary hypersecretion of gastric juice, with which it has many symptoms in common, by the presence of a hyperacidity during the early period of digestion, but which tends to become normal at that period when test meals are ordinarily withdrawn. The treatment of the condition should be largely directed toward the management of the nervous system. In emaciated individuals the best results are obtained by means of a systematic rest-cure treatment. The diet should consist largely of three meals a day, together with intermediate feedings of liquid food. The dietary should contain an excess of proteids and fats, and but a moderate quantity of carbohydrates. Of the various proteid foods, milk, eggs, and fish are to be preferred.

Fats have a tendency to decrease the gastric hyperacidity, and are to be recommended. Of these, butter, cream, and olive oil are especially useful. The carbohydrates are only permissible in the most digestible forms, and vegetables should be mashed and strained and taken in the purée form, free of all cellulose. Water is usually well borne, and may be administered in large quantities, with benefit. All acid food, as well as stimulants, should be avoided. The alkalies, together with belladonna, are of great service in the treatment of this disorder. Good results are usually obtained from the use of hydropathic measures, as well as from massage.

Case I.—F. R., male, aged twenty-six years, has been suffering with nervous exhaustion and gastric distress for three years; at times the discomfort would disappear for a period of from two to three

months, and would usually reappear after some nervous strain, or excitement. The symptoms are largely of a nervous character, consisting of irritability, headaches, and insomnia. There is, in addition, pain and pressure in the stomach one hour after meals, and extending over a period of from one to one and one-half hours. The pain is completely relieved by the ingestion of food. There are present acid eructations, heartburn, nausea, but rarely vomiting of acid matter. The pain is at times intense, and the patient often has a fear of eating. Tenderness can nowhere be detected, and occult blood is never present in the stools or gastric contents, and the stomach is in normal position and not dilated. The quantity of gastric contents obtained after an Ewald test breakfast is large, varying between 240 and 310 c.c., with a specific gravity of from 1010 to 1014, of a total acidity of from 40 to 48 and free hydrochloric acid from 32 to 38; the amidulin reaction is marked, and the proportion of solid sediment to fluid sediment is as 14 to 86. The height of digestion appears in thirty-five minutes, with a total acidity of 64 and free hydrochloric acid, 55. After a Riegel test dinner, the height of digestion appears in one hundred minutes, with a total acidity of 68 and free hydrochloric acid 62. The patient improved in health, under a carefully regulated diet, exercise, and massage, and the use of magnesia with belladonna.

Case II.—L. K., male, aged thirty-nine years, complains of gastric distress and nervousness for a period of over two years. In addition to the nervous symptoms, there is present much distress in the stomach one hour after meals, continuing about an hour; heartburn, acid eructations, and occasionally nausea are also present on examination, tenderness cannot be elicited anywhere over the abdomen; there is a splashing sound in the region of the stomach, and an enteroptosis is revealed. After an Ewald test breakfast an amount of gastric contents is withdrawn, varying between 250 and 334 c.c., of a specific gravity of from 1010 to 1013, with a total acidity of from 46 to 56 and free hydrochloric acid 36 and 40, and the proportion of solid to fluid sediment is as 15 to 85. The height of digestion appears in thirty-five minutes, when the total acidity is 65 and the free hydrochloric acid 55. After a Riegel test dinner the height of digestion appears in ninety-five minutes, with a total acidity of 65 and free hydrochloric acid 60. Under a partial rest treatment, together with dietetic restrictions and the use of belladonna and bicarbonate of soda, the patient was greatly relieved of his discomfort.

Case III.—M. G., male, aged forty-two years, has been suffering with nervousness and gastric distress for over six years. There is present insomnia, depression, and irritability, together with pain in the stomach, appearing one hour after meals, and continuing for about one hour, which is temporarily relieved by the ingestion of food. In addition, the patient complains of acid eructations, nausea, vomiting of acid secretion, heartburn, distention, flatu-

lency, and marked constipation. On examination, nothing abnormal can be detected in the abdomen. The stomach is in normal position, and nowhere can pain be elicited on pressure. After an Ewald test breakfast the quantity of gastric contents removed is large, ranging between 215 and 284 c.c., with a specific gravity from 1010 to 1014. The total acidity varies between 42 and 50 and and free hydrochloric acid between 34 and 44; the amidulin reaction is present, the proportion of solid to fluid sediment is as 18 to 82. The height of digestion appears in thirty minutes, with a total acidity of 68 and free hydrochloric acid 60. After a Riegel test dinner the height of digestion appears in ninety minutes; the total acidity is 70 free, hydrochloric acid 66. Under carefully regulated dietary restrictions, exercises, and hydrotherapy the patient improved for a short time, but, however, soon lapsed over into his former condition.

Case IV.—S. H., female, aged thirty-seven years, was suddenly affected with her present disorder following an intense shock. There appeared almost at once marked depression, restlessness, and irritability, together with nausea, fulness, and intense pain, appearing within an hour and a half after meals. The pain is temporarily relieved by the ingestion of food. The appetite remains good, but the patient has a fear of eating, due to the distress which is occasioned by the taking of food. Heartburn, acid eructations, and flatulency are also present. Physical examination reveals nothing abnormal, except a marked succussion sound in the region of the stomach, revealing an enteroptosis. After an Ewald test breakfast from 312 to 368 c.c. of gastric contents are obtained of a specific gravity, varying between 1011 and 1014, the total acidity varying between 38 and 40 and the free hydrochloric acid between 30 and 32; the amidulin reaction is marked. The proportion of solid to fluid sediment is as 16 to 84. The height of digestion appears in thirty minutes, when the total acidity is 65 and free hydrochloric acid 60. After a Riegel test dinner the height of digestion appears in one hundred minutes, when the total acidity is 68, and free hydrochloric acid 64. Under a strict rest cure, with the use of belladonna and the alkalies, the patient was almost entirely relieved of all discomfort after a treatment of eight weeks.

Case V.—L. T., male, aged fifty-eight years, has been suffering with nervousness and gastric disturbances for many years. He has been affected with great weakness, lassitude, exhaustion, depression, and insomnia, together with nausea, vomiting of an acid secretion, heartburn, pain, and discomfort one hour after meals. The appetite is normal, but the patient fears eating, owing to the distress caused by food. Nothing abnormal can be detected on physical examination. After an Ewald test breakfast from 252 to 298 c.c., gastric contents are obtained of a specific gravity of from 1010 to 1014, with a total acidity of from 50 to 56 and

free hydrochloric acid from 34 to 38. The proportion of solid to liquid sediment is as 15 to 85. The amidulin reaction is marked. The height of digestion appears in thirty minutes when the total acidity of the gastric contents is 62, and free hydrochloric acid 56. After a Riegel test dinner the height of digestion presents itself in one hundred minutes, the total acidity being 70, and free hydrochloric acid 62. Under careful dietetic regulations, with massage and hydrotherapy, together with the administration of alkalies, the patient gradually recovered his health.

Case VI.—P. M., female, aged forty-six years, reported for the relief of a condition from which she had been suffering from time to time for a period of over ten years. Her symptoms at first were those of a general neurasthenia, but three years ago her digestion became involved in addition to the general nervousness. The symptoms complained of are fulness and distention and pain after meals, with nausea, and vomiting of an acid secretion, with heartburn and acid eructations. The symptoms have recently become more intense, and the pain now is almost unbearable. The pain appears in from three-quarters of an hour to one hour after meals, and is relieved temporarily by the ingestion of a small amount of nourishment, but better by the use of bicarbonate of soda. On examination nothing abnormal can be detected. After an Ewald test breakfast from 325 to 340 c.c. of contents are obtained, with a specific gravity varying between 1011 and 1014; of a total acidity varying between 48 and 56, and free hydrochloric acid between 40 and 42. The proportion of solid to liquid sediment on centrifugalizing is as 14 to 86. The height of digestion appears in thirty-four minutes, with a total acidity of 65, and free hydrochloric acid 60. After a Riegel test dinner the height of digestion appears in ninety minutes, with a total acidity of 74, and free hydrochloric acid 65. The patient was placed on a carefully conducted rest cure, continuing over a period of six weeks, and entirely recovered her health.

AMYOTONIA CONGENITA: A CLINICAL AND PATHOLOGICAL STUDY.

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The disease called by Oppenheim[1] "myatonia congenita," but for which the term "amyotonia congenita" is rather to be preferred,

[1] Monatsschr. f. Psychiat. u. Neurol., 1900, viii, 232.

as less liable to cause confusion, was first described only eleven years ago. Since that time it has continued to arouse much interest, although its nature and true position among diseases are still not well understood and the number of reported cases is not great.

It consists, in brief, as originally described by Oppenheim, of a flaccid paralysis, apparently congenital, most marked in the extremities, especially the lower, and varying in degree up to almost complete paralysis of the whole body. There is no actual atrophy visible; the sensation is not disturbed; the tendon reflexes are diminished or abolished; the electrical contractility is much diminished; the hypotonia is so great that there is unusual passive mobility at the joints, and in bad cases the child is unable to sit and the head falls loosely in any direction.

One of us (Griffith[2]), in reporting, in May, 1910, a new case, that of Charles K., was able to collect and detail in abstract form but 48 other instances which seemed properly to belong in this category. In this article a study of the symptoms and pathological findings in the reported cases was also made and a bibliography appended. Some years earlier one of us (Spiller[3]) had published a personal case with the post-mortem findings. This was the first case reported in this country, and the first with necropsy reported by anyone.

Since the publication of the history of Charles K., above referred to, the child died, and we were fortunate in securing an autopsy. This is the second case with autopsy occurring in America. It is our purpose in the present paper to analyze briefly the clinical data given in the reports of cases published since the writing of this article, so far as known to us, and to discuss the pathology of the disease in the light of the findings in our own cases and in those of others.

Among the cases to be considered here we include those of Ashby and of Moussous and Carles, referred to in a footnote, but not analyzed in the earlier publication.[4] In giving these and other abstracts we have pursued the method employed in this publication, numbering them in continued series with those there detailed, and discussing symptoms briefly; this clinical portion being by way of an appendix to our earlier study of 49 cases (Griffith).

Case L.—Ashby.[5] Girl, aged eight years; family history negative; dated from birth. In bed, almost completely paralyzed; all muscles extremely flabby and wasted, including those of the face, which has little expression; can barely move limbs; cannot sit; some difficulty in mastication; reflexes absent or feeble; electrical reactions normal; intelligence somewhat impaired. Improved slightly under treatment.

[2] Archiv f. Kinderheilk., 1910, liv, 241; also Trans. Amer. Ped. Soc., 1910.
[3] Univ. Penna. Med. Bull. 1905, xvii, 342.
[4] Griffith, loc cit.
[5] Arch. of Pediat., 1910, xxviii, 363.

This case is in many respects anomalous, especially in the extreme wasting and the unimpaired electrical reactions.

CASE LI.—Moussous and Carles.[6] Girl, aged four years and three months; family history negative; dated from birth. Cannot walk; can move arms slightly and feebly; cannot sit erect or roll over; face seems a little inert; no apparent atrophy but muscles soft; electrical contractility lessened; no reaction of degeneration; intelligence a little diminished.

CASE LII.—Naish.[7] Boy, aged four years and eleven months; family history negative; dated from birth.

Examination. Hypotonia of all muscles of the trunk and limbs, but especially of the upper limbs; sits, with kyphosis; stands and walks uncertainly; all movements weak; knee-jerk almost absent; electrical reactions diminished; great passive hypermobility; intelligence normal.

CASE LIII.—Openshaw.[8] Boy, aged seven years and six months; could move arms and legs until measles at eighteen months, since then no power in legs; never walked; power in arms diminished slightly, but can write legibly; sits, with lordosis; cannot hold head up; decided wasting of muscles in arms, nothing said about legs; knee-jerk absent; contracture at hips, knees, and ankles; passive hypermobility of elbows; intelligence normal. "The muscles of the legs reacted to faradaic, and gave a brisk contraction with the constant current." Improved decidedly under treatment.

Biopsy of a portion of hamstring muscle showed "fatty infiltration; absence of cross-striation; irregular clefts with granular debris, with signs of regeneration in various parts."

The history as given leaves open some element of doubt regarding the diagnosis. It is not clearly stated whether the condition was congenital. The apparently sudden development, or rapid increase, of loss of power in the legs following measles, and the wasting in the arms are also not in accord with the usual picture of amyotonia congenita.

CASE LIV.—Zahorsky.[9] Boy, aged two years and three months; could not walk; knee-jerk diminished; no electrical contractility; "everything very flaccid." Improved somewhat.

The author designates this a case of myatonia, but the very meagre details given in the brief society report leave the important diagnostic symptoms unstated. Possibly a fuller account will appear elsewhere.

CASE LV.—Skoog.[10] Girl, aged twenty-two months; family history negative; could sit and support head at six months; never

[6] Arch. de Méd. des Enf., 1910, xiii, 472. From Jour. de Méd. de Bordeaux, 1909, No. 44, 697.

[7] Proc. Royal Soc. Med., 1909-10, iii, Neurological Section, 95.

[8] Ibid., Clinical Section, 39.

[9] Amer. Jour. Obstet., 1910, lxii, 1132.

[10] Jour. Amer. Med. Assoc., 1910, lv, 364.

crawled or attempted to walk. Disease not noticed by parents until fourteenth month.

Examination. Partial flaccid paralysis of arms and legs; all movements weak; cannot walk except a few steps when supported; holds head erect; sits, without kyphosis; possibly slight weakness in muscles of facial nerve; excessive hypermobility on passive movement; well nourished; muscles soft; tendon reflexes abolished; feeble galvanic and faradic response in some muscles, not in others; no reaction of degeneration.

Microscopic Examination of Muscle. Small piece of gastrocnemius removed. A section from immediately beneath the muscle sheath contained no muscle bundles, all being substituted by fatty tissue. A deeper section contained some small, pale muscular tissue and much fat; "some muscle fibers in process of destruction, and seem ending in continuity with substituted connective tissue;" much fatty tissue between bundles; no hypertrophied fibers; all quite uniformly atrophied; great nuclear proliferation. Blood-vessels have greatly thickened walls.

The history of this case leaves some doubt about its exact nature. Strongly against the diagnosis of congenital amyotonia is the absence of a positive history of congenital origin. This makes it seem possible that the disordered condition developed later and had been an advancing one. On the other hand, more careful observation by the parents might have thrown a different light on the case.

Case LVI.—Hummell.[11] Boy, aged three years; family history negative; dated from birth; never crawled or walked. Cannot stand; sits, with kyphosis; head falls forward when fatigued; moves legs, although feebly; upper extremities involved, but less so; decided passive hypermobility; muscles soft; tendon reflexes abolished; slight diminution of galvanic and great diminution of faradic contractility; no reaction of degeneration; no contracture. Ten months later there was decided improvement and he could stand with assistance.

Case LVII.—Chéné.[12] Girl, aged six months; family history negative; fetal movements felt; paralysis noticed by mother at end of second month, but disease probably congenital.

Examination. General flaccid paralysis; head falls any direction; kyphosis; cranial nerve supply normal; slight movements of hands and feet; limbs of normal size, but muscles feel soft, and fatty cutaneous tissue prevents determination of actual atrophy; extreme passive hypermobility of joints; knee-jerk and ankle-jerk absent; sensation and intellect normal; faradic contractility much diminished; galvanic response only with ten milliampères.

Case LVIII.—Chéné,[13] second case (unpublished case under care of Comby). Boy, aged ten months; family history negative;

[11] Jour. Nerv. and Ment. Dis., 1910, xxxviii, 719.
[12] Thèse de Paris, 1910.
[13] Ibid.

dated from birth. General feebleness of musculature; head supported with difficulty; moves limbs while lying in bed but ceases when lifted up; has difficulty in keeping himself erect when held on nurse's arm; muscles soft, no positive atrophy; no paralysis or contracture; knee-jerk diminished; passive hypermobility of ankles. Very large fontanelle and thorax flattened at the sides; rachitic rosary. In two months improved very greatly; could stand holding to objects; could hold objects in hands; knee-jerk present.

This case was carefully observed by a physician (Comby) with experience in this disease, and is doubtless a genuine one. The report, however, does not make it clear that decided, early rickets was not a factor of importance.

Chéné, in his list of cases, included one reported by Gayarre,[14] of which we have not seen the original report, but from the brief extract given the case hardly appears to belong here, inasmuch as exaggerated reflexes and clonus were prominent symptoms.

Case LIX.—Pollak.[15] Boy, aged six months, family history negative; fetal movements felt; dated from birth; arms and legs affected at first, but arms have improved somewhat.

Examination. Head falls to side as in newborn; marked kyphosis; respiration entirely abdominal; tone of abdominal muscles diminished; upper and lower extremities show flaccid paralysis; arms and toes move slightly on strong stimulation; muscles soft, not surely atrophied, as fat covering is well developed and prevents examination; movements of muscles supplied by facial nerves decidedly diminished, as seen when child cries; sucks with little power; muscles supplied by hypoglossal nerves much involved, and tongue can be depressed by finger with great ease; great passive hypermobility of joints; tendon reflexes absent; no electrical reaction of muscles or nerves obtained; sensation normal. Improved decidedly in course of a month, but died three months later of "capillary bronchitis." Thymus found enlarged. Later report of autopsy to follow.

Case LX.—Variot and Chatelin.[16] Girl, aged three and one-half years; family history negative; symptoms noted at six months; said to have been worse at two years than when reported.

Examination. Can make different movements with legs, but feebly; upper extremities involved but to less extent; sits, with kyphosis; cannot stand; holds head erect; passive hypermobility; thoracic movements normal; muscles soft without evident atrophy; tendon reflexes abolished; slight contracture at hip; faradic contractility almost abolished, galvanic much diminished; slight suspicion of degenerative reaction, but probably not genuine; intelligence normal.

[14] Revista Clin. de Madrid, June 15, 1909.
[15] Archiv f. Kinderheilk., 1910, liii, 373.
[16] Rev. Neurologique, 1911, xix, 138.

The almost certain congenital origin and the decided improvement make this a well-marked case, the positive reaction of degeneration not being certain enough to become an element of doubt.

Eleven additional cases, of which the abstracts have been here given, possibly belonging to the category of amyotonia congenita, have, therefore, come to our notice since the report of Charles K., and the analysis of other cases reported up to that date. This does not include two cases referred to by Cassirer,[17] of which we have no details. The cases vary in severity, and agree in the main with the general symptom complex of the disease. Inheritance of any family predisposition was not mentioned in any of them. In all, the disease began at an early age, the symptoms dating clearly from birth in the majority, and probably so in Chéné's first case. In Skoog's patient the symptoms were first noticed at fourteen months, and in Variot and Chatelin's not until six months. This may be through failure of careful observation on the part of the parents. In the cases of Openshaw and of Zahorsky the reports do not make the matter clear. In Openshaw's case the occurrence of an acute disease (measles) certainly made the weakness worse at eighteen months, if it had existed previously, while in Chéné's second case the process of recovery from the well-marked rachitis may have some bearing, to an extent not clear, upon the unusual and rapid improvement in the symptoms exhibited.

Muscular hypotonia was present in the lower extremities in all the 11 cases. Walking unaided was impossible except in Naish's case. In some cases, of course, the early age of the patient at the time the report was made precluded the possiblilty of walking in any event. The arms were more or less involved in all cases, but generally less than the lower extremities, as far as data are given on this point. Only in the case of Naish was the trouble greater in the upper extremities. In Oppenshaw's patient there appeared to have been very little affection of the arms.

When sitting was possible, as it was in about half the cases, spinal curvature was liable to appear. The face is reported involved in the cases of Ashby (little expression), Moussous and Carles (a little inert), Skoog (possibly slight weakness), and Pollak (decided diminution of motion, with involvement of the hypoglossal nerve). This is an unusual proportion in comparison with that generally reported, involvement of the cranial nerves being uncommon. Interference with thoracic respiration is mentioned by Pollak only. Decided hypermobility on passive movement is referred to in 9 cases. In the other 2 cases (Ashby and Zahorsky) no reference is made to the matter. No certain wasting of muscles was discovered, except in the cases reported by Openshaw and Ashby,

[17] Handb. der Neurol., Lewandowsky, 1911, ii.

but it is often stated that although the limbs seemed properly rounded, they were evidently soft, and the presence of the fat layer prevented the existence of atrophy being determined. The patellar reflexes were absent or greatly diminished in all cases except that of Moussous and Carles' patient. The original of their publication was not accessible to us, but at least no reference was made to it in the abstract. The electrical reactions were diminished in 8 of the 11 cases. In Chéné's second patient no reference is made to them; in Ashby's patient they were found normal, this case being anomalous in that as in other respects; and in Openshaw's case there would appear to have been no diminution, but the matter is not quite clear. A suspicion of a degenerative reaction was found in Variot and Chatelin's patient, but the condition was considered not a genuine instance of it. Some diminution of intelligence was reported by Ashby and by Moussous and Carles, but was evidently not of moment, and must be considered accidental, or apparent only. Contracture was present in the cases of Openshaw and of Variot and Chatelin. More or less improvement is said to have taken place in 7 instances. In Ashby's and Zahorsky's patients it was slight; in Openshaw's, Hummell's, Pollak's, and Variot and Chatelin's it was decided; in Chéné's second patient it was so great that it appeared to be largely due to improvement in the rachitis present. Only 1 death was reported (that of Pollak's patient) due to respiratory involvement, as has so often been the case in this disease. This was the cause of the fatal ending in our patient, Charles K.

The history of Charles K. up to the last notes made at the time of reporting is, in abstract, as follows:

Boy, aged fifteen months; admitted to the Hospital of the University of Pennsylvania, December 8, 1909. Parents, drunkards. Child had general flaccid paralysis from birth, and had never been able to use his legs or handle objects. Examination showed inability to sit or (Figs. 1 and 2) to hold his head erect; only very slight movement of arms and legs possible; diminished expansion of the thorax; no rickets, no wasting of the limbs; knee-jerk absent; moderate passive hypermobility of joints; slight contracture; entire failure of faradic and galvanic response. Under treatment up to April 26, 1910, the child improved considerably.

The later history of the child reads: During the month of May, 1910, the boy had more or less fever; there was decided improvement in the ability to hold the head erect, but he could sit only when propped with pillows. The abdominal reflexes were absent; respiration was still almost entirely abdominal; the slight contracture previously mentioned persisted. Anemia was decided, and this, with irregular temperature, continued until July. He was then sent to the seashore, but returned in September in about the same condition as when he left the hospital Little change of any sort took place, and there was certainly no improvement from this time.

About the end of October, 1910, he developed bronchitis, with fever, then pneumonia, and died after an illness of five days.

The autopsy was performed by Dr. B. S. Veeder, and his report and our findings in the nervous and muscular tissues are the basis for the statements which follow:

FIG. 1.—Photograph of Charles K.

FIG. 2.—Photograph of Charles K.

General. Body of a white male infant, about two years of age. The body was well nourished; no emaciation present; postmortem rigidity absent; practically no lividity; no scars or external markings. The skin was very pale, soft, and delicate in texture; no enlargement of the superficial lymphatics present; fontanelles closed. The autopsy was performed at a private house, under circumstances which made several features rather unsatisfactory.

Incisions were made in order to obtain nervous and muscular tissue. On incision of the calf the subcutaneous fat was found markedly

increased, and measured 1.5 cm. in thickness; the bloodvessels showed as pale white cords; the muscle tissue markedly atrophic, being rather tendinous in character, of a very pale color, and soft and flabby in consistency. A similar condition was found in the forearm, where the muscle surrounding the bone was simply a thin layer about one-eighth inch in thickness, the rest of the arm, which was of about normal size for the age of the child, being made up of adipose tissue.

Abdomen. On opening the abdominal cavity the fascia and subcutaneous tissue were found thickly infiltrated with a large amount of adipose tissue; the abdominal muscles little more than a thin sheath of tissue; the intestines distended, pale white, glistening in color, without adhesions; the liver extended slightly below the costal margin; no fluid present in the abdominal cavity. The abdominal wall showed a slight greenish discoloration of putrefactive change.

The spleen was moderately firm in consistency; maintained its shape when laid upon a flat surface; weight, 26 grams; sharp edges, rather pale red in color, smooth capsule, measured 7.5 x 4 x 2.5 cm. The cut surface was rather pale, not very moist, bled slightly, and showed faint markings of trabeculæ and follicles.

The liver was of firm consistency, with sharp edges, smooth capsule, of pale reddish-brown color, weighed 460 grams, and measured 18 x 11 x 5 cm.

The pancreas was dark purple in color, of normal consistency, and 8.5 cm. in length.

The stomach was decidedly distended, the mucosa thin, rather atrophic, grayish in color; covered with considerable mucus, and without ulceration.

A small portion of the ileum was removed for microscopic study, but only the duodenum was examined in its extent. This showed a thin wall, with the mucous membrane slightly grayish in color and without ulceration.

The right kidney weighed 70 grams and measured 10 x 4 x 3 cm.; was firm, rather bulging, and cut with normal resistency. The cut surface was smooth, and showed slight thickening and overgrowth of the cortical portion, which was pale white, and stood out in marked contrast to the dark red, congested pyramids. Throughout the kidney there were numerous small, grayish-white points, particularly in the pyramids and in the pelvic portion. The glomeruli were not visible. The vessels of the cortex showed distinct striation.

The adrenals were small, pale, and distinctly yellow in color.

The mesenteric lymph nodes were about the size of split peas; those of the retroperitoneum were not enlarged.

Thorax. Both pleural cavities were free from adhesions, but a few adhesions bound together the lobes of the right lung. The peri-

cardial sac was free from adhesions or fluid. The lower lobe and almost the entire upper lobe of the left lung were moist, dark blue in color, and firm; the rest of the lung exceedingly pale and crepitant throughout. The pleural surface showed markings of the alveolæ. Section of the dense firm area showed a deep blue, almost cyanotic color; the surface moist and exuding on pressure small white plaques of purulent material, with very slight bleeding. Section of the pale, soft, crepitant areas showed a rather normal appearance, except for quite marked anemia. The right lung weighed 180 grams; both the upper and lower lobes were involved in a bronchopneumonic process similar to that described in the other lung. The middle lobe was uninvolved.

The heart weighed 80 grams. The small, white, firmly contracted chambers contained small, firm, currant-jelly clots attached to the papillary muscles. The right ventricle contained soft clots in addition. The valves and orifices were normal in appearance. The musculature of the heart was rather pale, yellowish gray in color, and of fairly good consistency. The papillary muscles, especially on the right side, were pale and short. The wall of the left ventricle measured 9 mm., and that of the right ventricle 3 mm. in thickness.

The aorta and bloodvessels exhibited no lesions.

The thymus gland was rather small, and extended downward beneath the sternum as far as the second interspace.

The thyroid gland was exceedingly small.

Nervous System. No excess of fluid was found within the skull. The brain substance was soft and the membranes somewhat congested.

The spinal cord exhibited a rather edematous appearance of the membranes, with some coagulated blood extending almost the entire length of the canal.

The following tissues were prepared for histological examination: heart, lungs, liver, pancreas, kidney, adrenal, small intestine, thymus, thyroid, voluntary muscle, brain, cord, and nerves.

Heart: The cut surface showed a normal pericardium and endocardium. The muscle-fibers lay closely together, and both longitudinal and cross-striation were distinct. There was a slight granular condition of the protoplasm present. The nuclei were regular and oval in shape, and with considerable polar pigment. The bloodvessels throughout were filled with erythrocytes.

Lungs: Sections taken from the non-consolidated portion showed a moderate amount of congestion of the alveolar walls with occasional areas of edematous material partially filling the alveolar spaces. Sections from the consolidated part of the lung showed large areas in which the alveolar spaces were filled completely with an exudate consisting of leukocytes and broken-down cellular material. In most of these areas several bronchi could be made out in which there was almost complete desquamation of the epithelium, and

the lumen filled with broken-down and disintegrated cells, and with leukocytes. Occasionally areas were seen in which the alveolar spaces were only partially filled and in which some air was still present. There was marked congestion throughout.

Liver: The capsule was normal, and there was no increase in the perilobular connective tissue. The central veins were empty, and only a few capillaries were injected. Throughout the entire lobule the liver cells contained large vacuoles, occasionally forming quite typical seal-ring cells. The lumen of the larger bile ducts was filled with faintly staining granular material.

Pancreas: The interstitial and periductal connective tissue was not increased in amount. The cells of the acini stained well and did not show degeneration. The islands of Langerhans were numerous and large and showed nothing abnormal.

Kidney: The capsule was thin and regular. There was no increase in interstitial tissue in any part of the kidney. The cells lining the convoluted tubules stained poorly, and appeared as if smeared with eosin. The protoplasm was slightly granular and cell outline very indistinct. The nuclei were small and regular, and were rather solid, and there had been no loss of nuclei. The free margins of the cells were slightly irregular, and encroached somewhat upon the lumen of the tubules. The capillaries between the tubules contained few erythrocytes. The glomeruli were large, and almost completely filled the spaces. There was no exudate in the spaces, nor were there any evidences of proliferation present. The nuclei of the tufts were numerous and densely packed together, as is usually found in a young kidney. The bloodvessels of the tufts were well injected. Throughout the section marked congestion was seen.

All of the changes were explainable by a condition of postmortem degeneration, but as the other organs did not show this to such a degree, it is possible that there had been a cloudy swelling present.

Adrenal: The capsule and interstitial tissue showed no abnormality. In the cortex the three zones were distinct. The medullary portion was compact, and contained several large bloodvessels with a clear lumen. The nuclei of the cortical cells were large and somewhat vesicular, and stained deeply. The protoplasm was highly granular and stained rather faintly, but the large vesicles so frequently seen were not present. The only noteworthy feature of the medullary portion was the absence of cells bearing chromatin pigment.

Small Intestine: The mucosa of the duodenum was in a decided state of postmortem degeneration. The submucosa showed marked hyperplasia of Brunner's glands, which in places composed over half the entire thickness of the intestinal wall. The cells of the glands were granular and somewhat disintegrated. The other layers showed nothing abnormal. The ileum showed likewise con-

siderable postmortem degeneration of the mucosa, without other changes of note in the section.

Thymus: The thymus had undergone but little involution, the fibrous tissue between the lobules not being marked. The lobules were densely packed with cells. These were chiefly small, deeply staining lymphocytes, but numerous large cells, with oval and vesicular nuclei, were present. The corpuscles of Hassal were not very numerous, and were not fully developed. In many places there were small collections of the larger cells noted in which the cells were beginning to group themselves in a concentric manner, and transitions from this stage to a quite typical Hassal's corpuscle could be distinguished. Numerous eosinophilic cells were present, and these showed some slight tendency to occur in groups. There was a marked congestion of the bloodvessels.

Thyroid: The thyroid showed nothing distinctly abnormal. In a few places there was a slight hyperplasia of the epithelial cells lining the acini, and although the acini were uniformly filled with considerable colloid material, there was no dilatation of them.

The gross anatomical diagnosis consisted then of atrophy of the muscles, with general fatty infiltration; bronchopneumonia; cloudy swelling and congestion of the kidneys, and slight cloudy swelling of the liver. The histological diagnosis, not including the muscular and nervous system, was bronchopneumonia, cloudy swelling of the kidney, and fatty infiltration of the liver.

As special interest attached to the condition of the muscular and nervous systems, we have given particular attention to this part of the pathological findings, with the following results:

The brain was unusually large, and appeared more like the brain of an adult than that of a child. It weighed 1542 grams after it had been one week in a 10 per cent. formalin solution. The cord measured 23 cm. in length, and as it had been removed close to the foramen magnum, the difference in the relative size of the brain and cord was striking. The posterior spinal roots appeared to be of good size, and a transverse section of the cord was not unusually small. The anterior roots throughout the cord were small.

The cells of Betz in the right and left paracentral lobules were numerous, especially in the left, although no significance is to be attributed to this apparent excess on the left side. In some of the Betz cells the chromophilic elements were in normal form; in others they had become granular. The cells of the hypoglossus nuclei may have been a little diminished in number, but there was no noteworthy atrophy comparable with that of the cells of the anterior horns of the spinal cord.

Sections from the seventh and eighth cervical segments showed few nerve cells in the anterior horns, except that in the eighth cervical segment a group of cells was present on each side corresponding to the intermediolateral tract. The few cells remaining

in the anterior horns were small, but contained chromophilic elements. No degeneration in the white matter was detected by the Weigert hematoxylin stain. The anterior horns by this stain appeared a little pale, as from a scarcity of nerve fibers.

The seventh and eight posterior cervical roots, cut separately from the cord, were in excellent condition, showing no degeneration. The anterior roots from these levels were degenerated, but somewhat less so than the anterior roots of the lumbar region. No evidence of degeneration by the Marchi stain could be found in sections from the cervical, thoracic, or lumbar region.

The anterior horns of the lumbar region were paler than the posterior horns. The nerve cells of the anterior horns were few, and most of those present were shrivelled. The cells of Clarke's columns were in good condition; some showed alteration—namely, chromatolysis and peripheral displacement of the nucleus—but such findings are not unusual in the cells of these columns.

The nerve cells of the anterior horns in the lumbar region did not show any noteworthy change by the Bielschowsky method. The first, second, and third anterior lumbar roots, cut separately from the cord and stained by the Weigert hematoxylin method, showed great diminution in the number of medullated fibers, and a considerable overgrowth of connective tissue was evident when acid fuchsin and hemalum were used for staining.

The first, second, and third posterior lumbar roots appeared to be normal. The difference between the anterior and the posterior lumbar roots was very striking, as the former were much degenerated.

Portions of muscle were taken from the back near the neck, from the forearm just below the elbow, and from the calf. The muscle from the forearm showed great atrophy of muscle fibers, but even these greatly atrophied fibers preserved their transverse striation, although longitudinal striation was not distinct. The atrophy affected certain bundles, and other bundles in the immediate vicinity in large measure escaped. The intramuscular nerve fibers stained by the Weigert hematoxylin method showed considerable degeneration, and in some nerve fibers the medullary substance appeared as broken into small black balls. Here and there in transverse section a bundle of rounded, unusually large muscle fibers was found. The atrophied fibers showed an excessive number of sarcolemma nuclei, in some places the nuclei forming dense masses, and almost obscuring the greatly atrophied muscle fibers. By careful examination the atrophied muscle fibers usually could be detected. The interstitial tissue was considerably increased. Some of the muscle fibers showed fatty changes within them by the Marchi method, in the form of minute droplets in small points.

Muscle from the back resembled that from the forearm, but was in better preservation; that is, the atrophy was not so intense.

There were many highly congested bloodvessels. Marchi's method revealed fatty degeneration within the muscle fibers, but not so much as in the muscle from the forearm. Intramuscular nerve fibers stained by the Weigert hematoxylin method appeared partially degenerated. Some large muscle fibers were found. Many muscle fibers appeared rounded in transverse section. Some muscle bundles were little affected, and yet were surrounded by bundles of greatly degenerated muscle fibers.

FIG. 3.—Section of a muscle from the back, showing the atrophy of many muscle fibers with a bundle of nearly normal fibers in the midst of greatly atrophied fibers.

The calf muscle was similar to that from the forearm, but the changes were more intense in the former. The muscle fibers were more atrophied, and the interstitial fibrous tissue was much increased in amount. The connective tissue nuclei were distinctly more numerous. Fatty change was evident by the Marchi method within many of the muscle fibers. There was an excessive amount of fat between them. A piece of nerve, probably the posterior tibial, cut with the muscle, showed much degeneration by the Weigert hematoxylin method. Intramuscular nerve fibers were considerably degenerated. The muscle fibers within the muscle spindles appeared to be normal. The bloodvessels within the calf muscle were much sclerosed.

A piece of the median nerve teased and stained with 1 per cent. osmic acid solution showed no pronounced degeneration by this method.

A summary of the important findings in the muscular and nervous systems in this case is as follows:

The brain was of extraordinarily large size for so young a child (twenty-five months), and was as large as that of an adult. Excepting the large size, it presented no gross anomaly. The nerve cells

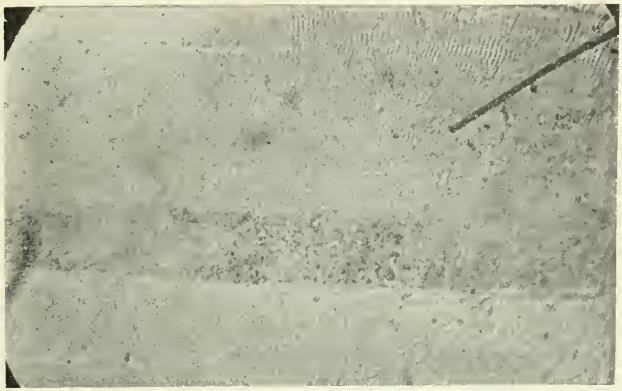

Fig. 4.—Section of muscle from the calf stained by the Marchi method, showing fatty change within a muscle fiber.

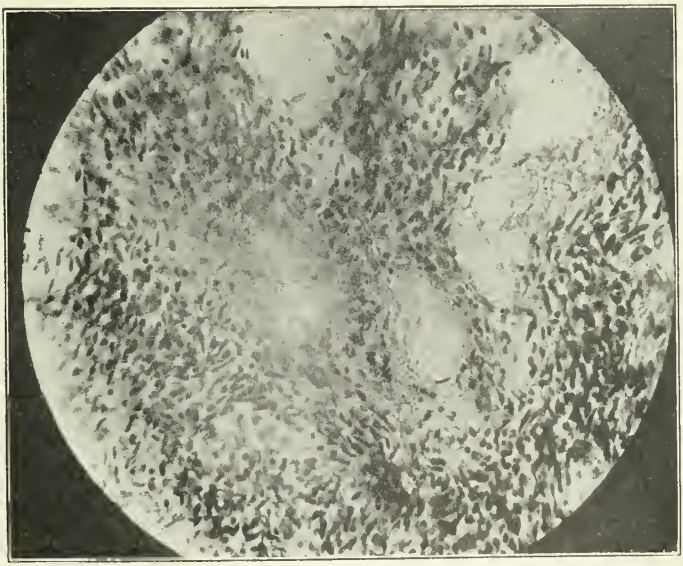

Fig. 5.—Section of muscle from the calf, showing the great excess of sarcolemma nuclei and connective-tissue nuclei and of fatty tissue.

of the anterior horns in the cervical and lumbar regions were scarce, and those present were much atrophied. The anterior roots throughout the cord were considerably smaller than in a normal

spinal cord, and stained imperfectly by the Weigert hematoxylin method. A peripheral nerve examined was much degenerated. The alteration of the muscles was intense, and consisted of greatly atrophied muscle fibers in the midst of other fibers well preserved, of overgrowth of sarcolemma nuclei and connective-tissue nuclei, of excess of fibrous and fatty connective tissues, of increase in size of some muscle fibers, and of fatty change within certain muscle fibers. The intramuscular nerve fibers showed degeneration. The muscle spindles appeared to be normal.

A comparison of this case and of its pathological findings with the case B. T., previously reported by one of us (Spiller), is instructive. The condition in B. T. corresponded closely with the description of the disease as given by Oppenheim. Objections have been made to it by one or two authors on two points—namely, a so-called blindness and a so-called paralysis of deglutition. Neither of these conditions was recorded in the history. The case has been accepted as typical by many, especially by such important investigators as Collier and Holmes, and Cassirer.

The baby was born at full term, and the birth was normal. It was breast-fed until the date of its admission to the hospital. Nothing abnormal in the child was noticed by the parents until he was about five months of age, when he did not seem to take notice of things as he should. He had never been able to hold anything in his hands. The mother had not noticed any increase in the child's weakness since birth, and as he was very weak when he came under the observation of one of us, it is reasonable to suppose the child was equally weak at the age of five months. The mother was an intelligent woman, and her statements were reliable. It is presumable that so marked a weakness might readily escape detection by the parents in the first months of life, and it is equally presumable that a child so weak would not notice objects in a normal manner. So far as the ocular examination can be relied upon it was negative, as shown by Dr. de Schweinitz's explanatory letter accompanying the published report.

The statement made in the report of the case might lead one to conclude that paralysis of deglutition existed, but probably such was not the case. The child was breast-fed until the time of his admission to the hospital, and had shown no difficulty in swallowing. When he was given cow's milk in an attempt to wean him he spit it out; in the report the words are, "And of late, since he has been taken from the breast, has swallowed with some difficulty."

It was not supposed that these words would be taken to mean a paralysis of deglutition. The child had swallowed well while on the breast. Inasmuch as he was twenty-two months of age, and possibly was not receiving sufficient nourishment, and also because it has been suggested that the development of amaurotic family idiocy may be dependent on the mother's milk (a view hardly acceptable),

it seemed advisable to endeavor to have the child nourished by cow's milk. That the child would not immediately swallow this, and later swallowed it unwillingly and apparently with difficulty, in no way proves a paralysis of deglutition, and probably such paralysis did not exist. Even if it had, it would not have weakened the diagnosis in any way. As the hypoglossus nucleus has been found affected in amyotonia congenita, it is not unreasonable to suppose that the nuclei governing deglutition some day may be found implicated.

As for the objection to the case based on the existence of a squint, that has already been answered in an article published several years ago.[18] The muscular condition was typically that of amyotonia congenita, and yet the degree of weakness was not so intense as in some of the reported cases.

The pathological findings in this case are important, and the examination was complete. If more findings were not recorded, it was because they did not exist, with the exception of some alteration of the muscle from the left foot, not observed in the sections made at the time of the report. Since that time new sections have been made from all the muscles obtained, but only in those from the foot were additional findings observed. The pathological findings are recorded here in order to compare them with the findings in the case of Charles K.

"The spinal cord and brain were well developed, and the anterior and posterior spinal roots were normal. The nerve cells of the anterior horns of the cervical and lumbar regions were normal by the theonin stain. The white matter of the spinal cord was not affected, even by the Marchi stain. A nerve from the upper part of the right upper limb stained by the Weigert hematoxylin or acid fuchsin method was normal. The internal popliteal nerve and a nerve from the upper part of the right upper limb teased and stained by a 1 per cent. osmic acid solution were normal.

"Muscles from the sole of the left foot, from the back of the trunk, and from the left calf had a hyaloid appearance, and that from the sole of the foot was striking, on account of the increase in the nuclei of its connective tissue. The muscle fibres were small, and those from the sole of the foot and from the left calf were much smaller than those from the back of the trunk, and the child had had more power in the muscles of the back than in those of the lower limbs. Unusually large muscle fibers were not observed. The transverse striations were well preserved, but the longitudinal were not so distinct. Nerve fibers within the muscles from the sole of the foot appeared to be normal."

It is difficult to know in what way the report of the muscular condition could have been enlarged upon.

[18] Spiller, Neurologisches Centralblatt, 1907, No. 11.

It was not asserted in the report of the case of B. T. that amyotonia congenita must be considered as a purely muscular disease. The statement was, "Congenital myatonia seems from the study of this case to be a muscular disease." It might have been well to italicize the words "this case," but it was not supposed that the statement would be taken to imply that one case could determine the pathology in all its details of a new disease.

The case of Charles K., reported in this present paper, was one of a more advanced type than that of B. T., and the findings were much more pronounced. In the former the nervous system, as well as the muscular, was greatly affected. In recently made sections from the left foot of B. T. some areas were found in which certain of the muscular fibers in bundles were more degenerated than any seen in previous sections, and these were in the midst of fibers of normal size. Some of the muscular fibers had disappeared in these areas. These findings were considerably less intense than those of the muscles in Charles K., and seem to present a transitional stage to the intense muscular degeneration of the latter case.

It is instructive to compare the findings in the reported cases. Beginning with the earliest, Spiller's case, the findings were purely muscular, and not intense although pronounced.

In Baudouin's case the changes in the nervous system appear to have been slight. In the lowest part of the eighth cervical segment the cells of the anterior horns were diminished in size and not so numerous; but one gets the impression that the diminution in number was not very great. Baudouin says: "Mais dans les groupes externes, où elles sont plus volumineuses, elles ne dépassent pas 25 microns de diamètre et sont plus rares qu'a l'état normal."

In Lereboullet and Baudouin's case the brain and cord were normal; no change in the cells of the anterior horns nor in the anterior or posterior roots was found. This case resembles that of Spiller in its findings. Some of the muscle fibers were very small, and some were very large.

In Collier and Holmes' report (case of Collier and Wilson), as well as in that of Rothmann, the changes were pronounced in the nervous system as well as in the muscles.

Reyher and Helmholz's findings were important, showing decided changes in the muscles, but no reference is made to the nervous system.

Microscopic examination of portions of muscle excised during life are reported in the cases of Bing, Collier and Holmes (first case), Openshaw, and Skoog. In the first there were practically no changes found; in the other 3 cases they were decided. These reports are of value as far as they go, but throw no light upon the frequency of involvement of the nervous system.

A finding, so far as we know, observed only in our case (Charles K.),

was the formation of fat within the muscle fibers, indicating that actual degeneration was progressing, and that the muscle change was not merely arrest of development.

From this review of the few cases as yet reported with necropsy, we may conclude that in the lighter cases (Spiller, Lereboullet and Baudouin) the alteration may be confined to the muscles, and possibly, therefore, the disease is primarily muscular, but this inference is not fully warranted. In the intense cases the nervous system is affected in marked degree. The relations to muscular dystrophy, as maintained by Batten, and to the Werdnig-Hoffmann type of muscular atrophy, as so ably set forth in Rothmann's excellent paper, are as yet undetermined. The points of resemblance to both these diseases cannot be ignored. Cassirer[19] in his recent paper has described amyotonia congenita so fully that little is left to be said upon the subject. A review of the literature is given by him, as also in the early paper by one of us (Griffith[20]), and of later cases in the present contribution.

We are indebted to Dr. Allen J. Smith for the photomicrographs.

THE TOXIC ACTIONS OF DIGITALIS ON THE HEART.*

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The object of this paper is to discuss the toxic effects of digitalis and associated bodies, to show the frequency of these effects in ordinary practice, and to urge that the administration of these drugs be more carefully controlled.

The observations upon which this paper is based were from 90 cases under treatment with digitalis or digitalis bodies on the several medical services of the second division of Bellevue Hospital. The administration of the digitalis drugs to these patients was conducted with great care, and improvement in the character and condition of the pulse, with relief from the symptoms, was the accepted indication for either stopping the drug or reducing the dosage. About 25 per cent. of the cases showed some form of toxic action. These observations were made during the course of another research, and many of them do not cover the entire period of the toxic action.

[19] Loc. cit. [20] Loc. cit.

* Tracings presented before the New York Academy of Medicine, Section on Medicine, in the annual report of the Second Medical Division of Bellevue Hospital, December 19, 1910.

In recent years the polygraph has been developed and popularized by Mackenzie and others, so that we now have clinical instruments (such as the Jacquet sphygmocardiograph, used to obtain the illustrations of this paper) presenting results which may be interpreted at the bedside. We have a means of investigating the action of the right and left chambers of the heart, of measuring the conductivity, of estimating the contractility, and of locating the origin of the beat.

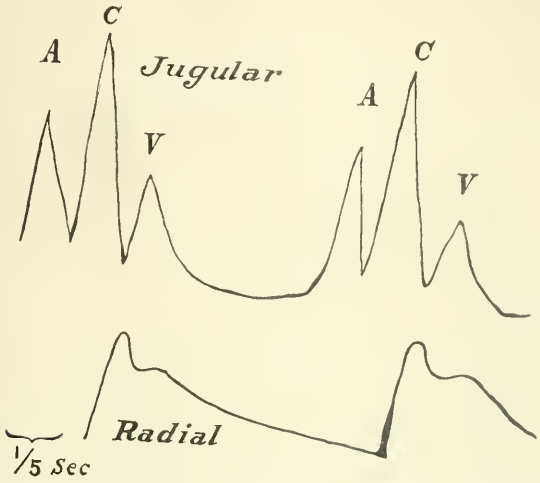
The administration of digitalis to a patient whose heart is exhausted by myocardial and valvular disease is a proceeding requiring great care. A number of factors prevent ideal results, and it is impossible to formulate rules, for the knowledge of how much digitalis each patient will be able to take with benefit cannot be obtained. Our present methods of estimating the total force and reserve force of a heart are inadequate, but hearts dilated and weakened by frequent losses of compensation should theoretically at least require less digitalis than those not so badly damaged.

The active principles in the preparation we use vary in amount, and when they are administered by mouth we are unable to say even under normal conditions how quickly absorption will occur, how much will be absorbed, and how much rendered inert by fixation, destruction, or removal by peristalsis. Even when a definite quantity of one of the glucosides, such as digitoxin, is given, the obstacles to its use by the mouth still remain, and it is well known that this principle is not suitable for subcutaneous or intramuscular injection. Our great need is for a readily absorbable principle having the digitalis action, for oral administration must continue for the present to be the method used in general practice, although crystalline gratus strophanthin (or ouabain, as it should be called) nearly fulfils the conditions when it is used by intravenous or intramuscular injection.

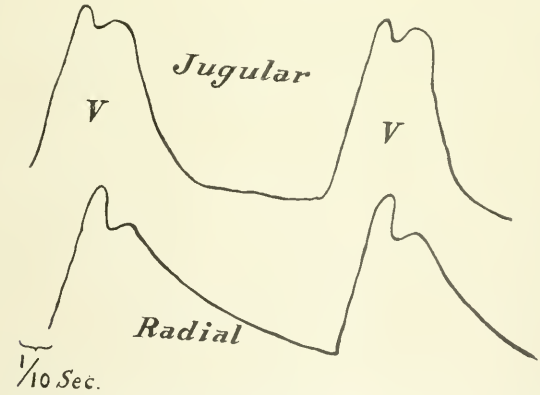
Observations of the effects on the cardiac functions afford the only method by which we can estimate the amount of these principles which is absorbed into the circulation. Jugular, apex, and radial tracings give a fair idea of the conditions of stimulus productions, excitability, contractility, conductivity, and tonicity, and also of vagus control.

It may be advantageous to consider briefly two types of pulse tracings which are frequently seen. The jugular pulse may be positive or negative, the normal or negative venous pulse having waves commonly termed *A*, *C*, and *V*, the positive pulse having one wave usually notched on its plateau, and termed the V wave. This wave *V* appears at ventricular time, and is either due to regurgitation through the auricularventricular valve or it is due to the ordinary *C* influence plus a late contraction of the auricle, when the auricularventricular valves are closed.[1 2] (Tracings 1 and 2.)

The chief actions of digitalis on the heart are due to (*a*) vagus stimulation, (*b*) direct effect on the myocardium, and (*c*) the influence of vasoconstriction. While the vagus action and the



Tracing 1.—Negative venous pulse (diagrammatic). *A* wave is due to the contraction of the auricle and occurs about one-fifth second before *C*. *C* wave is due to the contraction of the ventricle and occurs one-tenth second before the radial pulse. *V* wave is due to the overfilling of the auricle before the tricuspid valves open, or to the closure of the semilunar valves and rise of pressure in the right ventricle.



Tracing 2.—Positive venous pulse (diagrammatic). Begins at *C* time, or one-tenth second before the radial. No auricular wave in the usual place.

direct cardiac actions are antagonistic they are intimately associated, and each has a bearing on the others, still the toxic effects may be divided into three stages which usually follow one another, and may be arranged in order of their severity as follows:

I. Period of vagus stimulation.

II. Period of depression of conductivity with masked vagus action.

III. Period of marked muscular irritability with depression of contractility.

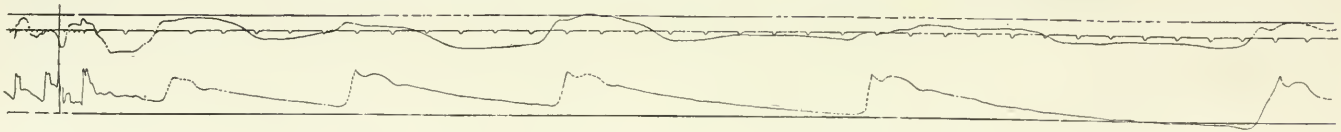
I. Period of Vagus Stimulation. The vagus action of digitalis is due chiefly to stimulation of the medullary centre, although the peripheral endings are also somewhat affected. It is usually the first perceptible action to develop, and is followed slowly by the increase of irritability of the musculature. The slowing may become so marked that syncope develops between contractions,[3] but the rate seldom falls below 45 per minute. As a rule, the slowing is counteracted by the increase in contractility, but death may result from failure of the circulation due to the diminished output of the heart. Before death this condition usually passes into one of severe muscular irritability.

There are two types of vagus action dependent upon the rhythm of the heart: (1) When the heart beat originates at the sinus and the *A, C, V* rhythm is present, the slowing is usually regular and the auricular-ventricular period (*A-C* interval) is normal, or about one-fifth of a second. (2) When the rhythm of the heart originates elsewhere than the sinus the ventricular beats are absolutely irregular. This condition was termed provisionally by Mackenzie "nodal rhythm," with the idea that the rhythm originates at the auricular-ventricular node.[4] Lewis[5] has recently shown that when this rhythm occurs the auricle is in a state of tachycardia with impulses to contraction starting at several places in the auricular musculature. Hearts with this rhythm remain absolutely irregular and the slowing alternates with contractions having normal or nearly normal diastoles. The vagus apparently has not such complete control over the auricularventricular node or other portions of the auricular muscle as it has at the sinus, and as a result a number of beats at the normal rate are followed by successively lengthening diastoles until a certain maximum is reached, usually in the course of two or three beats, then these contractions are, in turn, followed by a few with successive shortening of their diastoles until the normal rate is again attained. (Tracings 3, 4, and 5.)

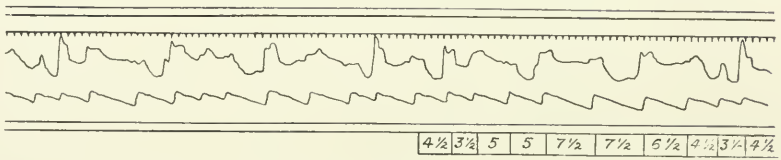
It is important to recognize this particular variety of vagus effect, because the seriousness of the condition is not indicated by the radial pulse rate, and these hearts pass rapidly from this period to one of marked muscular irritability with the presence of coupled beats, which is far beyond the therapeutic stage. During the administration of digitalis by the mouth to patients with this rhythm, tracings should be taken at least once in twelve hours.

II. Period of Depression of Conductivity with Masked Vagus Action. Changes in conduction occur in acute fevers, especially in rheumtaic fever, from local lesions in the His bundle,

Tracing 3 (H. C., November 5, 1909).—Vagus slowing with normal *A*, *C*, *V* rhythm. Upper tracing jugular, lower radial. Rate 45. *A-C* interval is normal. Increase in the contractility may be noted by the rise of the lever in systole. Cardiac output unimpaired.



Tracing 4 (R. J., January 9, 1909).—Vagus slowing in auricular fibrillation. Upper tracing jugular, lower radial. Gradual lengthening of the diastolic periods.



Tracing 5 (J. O'H., November 8, 1909).—Upper jugular, lower radial. Gradual lengthening and then shortening of the diastolic periods. Phenomenon of vagus control in auricular fibrillation.

and possibly from marked vagus stimulation when all the functions of the heart are depressed. Digitalis heart block generally accompanies changes in other functions, so that differentiation is not difficult, especially if tracings were taken previous to the administration of the drug. Mackenzie believes changes in conduction occurring under digitalis treatment are the result of the action of the drug on the vagus;[6] but for the following reasons I believe it is due to the myocardial condition itself.

1. When there is evidence of marked vagus stimulation with stoppage of the entire heart for two or more seconds the following auricular wave is conducted in normal or less than normal time to the ventricle. In other words, when vagus action is most prominent, conduction time is normal or lessened, presumably from the length of time the muscle is at rest. (Tracing 6.)

2. Changes in conduction may occur when apparently no vagus effects are present. Examples are seen in loss of conduction from sinus to auricle and the production of a type of pulse often seen in digitalis poisoning, and furthermore frequently produced in animal experimentation. (Tracings 7, 8, and 9.)

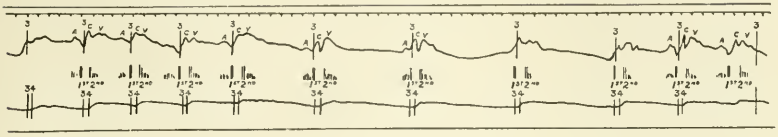
3. Delay in the *A-C* interval may occur in hearts which are slowed only by a time equal to that delay. Hearts which show marked conduction changes have decided slowing, that is, the diastolic periods are considerably prolonged. It may be shown that this diastolic prolongation is only equal to the delay in the *A-C* interval. (Tracing 10.)

4. Complete heart block in digitalis poisoning occurs with the auricle beating at a very rapid rate or when the irritability of the auricular muscle entirely masks vagus action. (Tracing 11.)

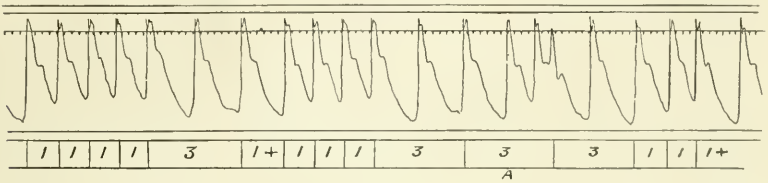
While the various forms of heart block produced by digitalis are grave evidences of toxicity and certainly produce an artificial condition which is serious as regards the maintenance of the circulation, still the milder forms at least are but little worse than marked vagus slowing. Many hearts show conduction changes followed by irritability of the muscle, apparently without passing through a stage of vagus slowing, but this is only apparent, and I believe careful watching will detect a transient stage of vagus action.

III. Period of Muscular Irritability. When the third period of the toxic action of digitalis and its allies is reached, the condition is serious because the total energy is markedly diminished and an extreme degree of loss of compensation results. It is impossible to differentiate certain stages of irritability from the progress of the cardiac disease, and these cases are the most important, because further administration of the drug may mean death.

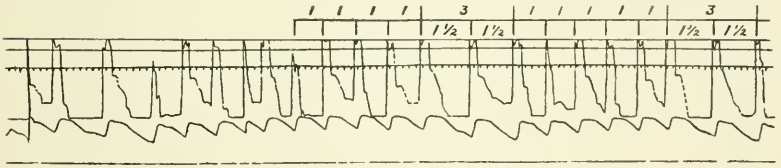
The first evidence of irritability of the muscle is the coupled beat or early extrasystole. This condition simulates veratrin poisoning of the muscles of the frog. The stimulus to contraction is



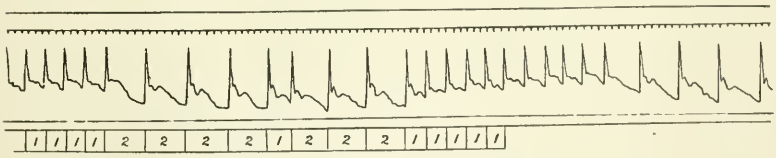
Tracing 6.—Tracing from Mackenzie's "Diseases of the Heart." Upper jugular, lower radial. Note the shortening and finally the absence of the *A-C* interval after the long pauses.



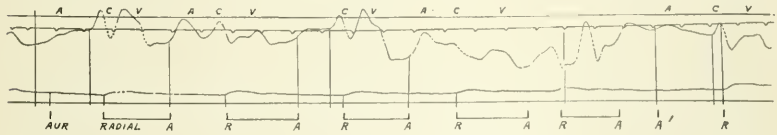
Tracing 7 (H M., February 2, 1909).—Partial block of impulse at sinus. At periods marked 3 there is delay at the sinus but the contractions finally go through. The impulse for the following contraction strikes the heart during the refractory period. At *A*. the first contraction is delayed at the sinus; so also is the second, which reaches the heart after the refractory period. The rhythm is picked up again by the peculiar systole, which appears like an extra systole, and the entire time is equal to three cycles, as in the other periods of slowing.



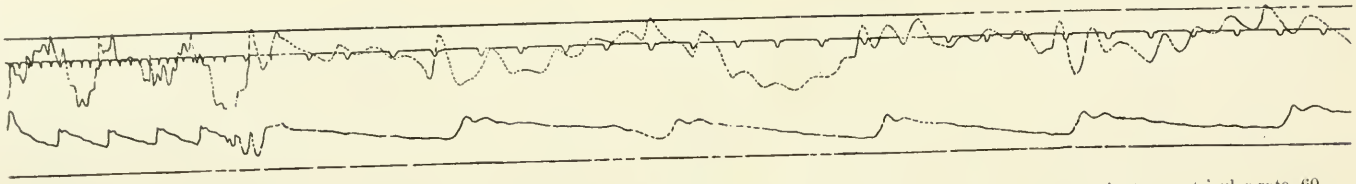
Tracing 8.—From the same case six days later, no digitalis in the interval, upper tracing jugular, lower radial. Occasional slow period as before. Partial block. The upper tracing may be carotid, but as there is a plateau at the top of the wave and a second notch even higher than the first it is probable that it is the positive wave of the jugular.



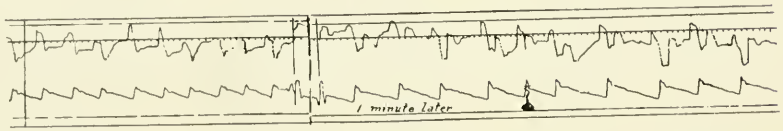
Tracing 9 (B. J., March 23, 1909).—Complete block at the sinus. During the intervals marked 2 an impulse at the regular time fails to reach the auricle. The rhythm is maintained.



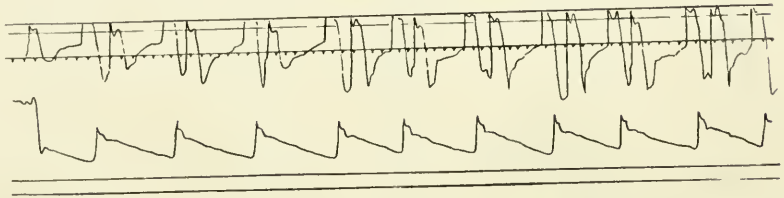
Tracing 10 (M. O'N., December 22, 1908).—Upper jugular, lower radial. Diagram beneath shows that the time between a radial pulsation and the next following auricular pulsation is always the same. Sinus rhythm is regular, radial pulse irregular. Slowing pulse rate entirely due to auriculoventricular block. At *A'* a complete block occurs.



TRACING 11 (J. K., March 31, 1910.—Upper jugular, lower radial. Complete heart block. Auricular rate, 350 to 390 per minute; ventricular rate, 60.



TRACING 12 (D. C., November 3, 1909).—Upper jugular, lower radial. Period of rapid pulse followed by slow coupled beat phenomena. These phasic changes occur constantly, and a pulse should be taken over a period of a minute or two.



TRACING 13 (J. R., January 12, 1910).—Upper apex beat, lower radial. Two contractions at the heart with but one pulsation at the wrist. Early extra systole. coupled beat phenomenon.

apparently prolonged over a considerable period, and as soon as the latent period has passed the heart again contracts.

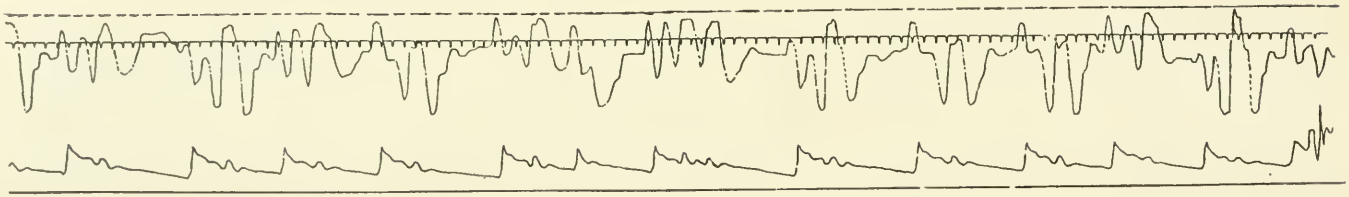
The theory of Bottazzi[7] in regard to the action of veratrin is interesting in that it ascribes to muscle two contracting substances, the fibrillary substance and the sarcoplasm, the first responding to ordinary stimuli and the second only to very strong stimuli. The second contraction occurs late or early, according to the degree of irritation. This theory accords very well with the facts in digitalis poisoning, for in hearts recovering from this rhythm the extrasystoles sometimes occur later in diastole.

As a rule, the early extrasystole is ventricular, but it is sometimes nodal and it may be a retrograde contraction. It is usually followed by a longer diastolic period than may be accounted for by computing the sum of two normal contractions; but it sometimes has a short diastolic pause, and when this occurs it is a serious omen, because there is no time for the contractile substance to reform, and there ensues a rapid bigeminal action of weak systoles with complete failure of compensation. (Tracings 12, 13, and 14.)

Mackenzie has shown that the coupled beat action is particularly common in cases of auricular fibrillation. It is not, however, the only type of irritability shown by these cases. They may pass rapidly from a condition of slowing to one of very rapid rhythm with more or less regularity, or into a condition of delirum cordis where no diastolic periods intervene between the contractions. The contractility is so markedly diminished under these circumstances that a great number of the beats are insufficient in force to open the aortic valves and cause a pulsation at the wrist.

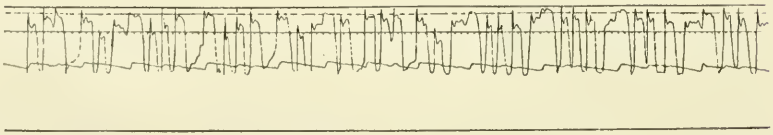
When this condition exists there may be present also the terminal condition of intraventricular heart block.[8] It is usually but partial, that is, while the fibers of one chamber contract with force, only a portion of the fibers of the other chamber contract, or else all contract feebly. There is often delay apparently between the time of contraction of the two chambers, the musculature of the right contracting a little later than that of the left side. (Tracings 15, 16, and 17.)

The vasoconstrictor action of the therapeutic dose of digitalis is probably slight, but some rise in blood pressure follows the use of the drug, especially where the pressure is low. This rise is chiefly due to increase in the force of the cardiac contractions. Where toxic doses are given, as in those cases where coupled beats occur, there is usually a considerable rise in pressure. This is very important, because the vasoconstriction occurs at a time when the heart is embarrassed by the irritation of the poison. Digitalis is said to constrict the coronaries, but, as Hatcher has said, it is impossible to believe that the food supply is lessened at the time the amount of work is greatly increased. Probably no considerable amount of constriction occurs with ordinary doses.



TRACING 14 (R. T., December 14, 1908).—Upper jugular, lower radial. Extreme example of the veratrin-like action. Stimulus to contraction at times lasts over one second, and three contractions occur. This tracing shows that the first contraction may be from the sinus and the second and third either from the node or retrograde. The slowing is due to delay in the *A-C* interval. There are no vagus effects present in the tracing.

TRACING 15 (F. H., February 7, 1909).—Upper tracing. First part jugular, second part apex. Marked muscular irritability of the heart (delirium cordis).



TRACING 16 (S., October 1, 1909).—Upper jugular, lower radial. Intraventricular heart block. Right ventricle contracting slightly behind left and many strong contractions on the right side effect the left not at all or only so feebly that the aortic valves are not opened.

Crystalline gratus strophanthin has less effect on the blood pressure than digitalis has, and even after toxic doses only a slight rise may be noted.[9]

With digitalis itself cumulative effects often occur, and evidences of muscular irritability may persist for considerable periods. Many patients who have developed the coupled beat continue to show this phenomenon for a week after the digitalis has been discontinued, and extrasystoles may be present as late as twelve days and perhaps longer. It may be that the continuation of a particular rhythm is not due to the presence of the original stimulus, but it seems likely, for unpublished results in this laboratory tend to show the persistence of the effects of the drug in cats as late as three weeks after its administration by vein.

Tracings 7 and 8 show persistence of sinus block six days after the medication had been stopped, and Tracings 18 and 19 show the continuation of the coupled beat action for eight days. (Tracings 18 and 19.)

Vomiting occurring during the course of the administration of digitalis by mouth is usually attributed to the irritant local effects of the drug on the gastro-intestinal tract, and frequently a change is made to some other digitalis preparation or to some other methods of administration.

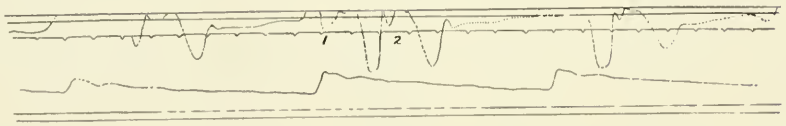
Control by heart tracings in man, together with experimental work on animals, leads us to the belief that vomiting from the digitalis bodies is almost wholly a central effect, and means, therefore, that absorption has occurred and further administration may lead to marked toxic action.

True pulsus alternans is said to be frequently caused by digitalis.[9] If the cases showing the coupled beat or early extrasystole are ruled out, I have never seen digitalis produce this type of pulse, but I have tracings from three cases where pulsus alternans existed and where the administration of digitalis bodies removed the condition. This pulse is caused by a lessening of the power of contractility due to change in the myocardium, and possibly may occur in severe poisoning with digitalis, but it is certainly not distinctive of that condition. (Tracings 20, 21, and 22.)

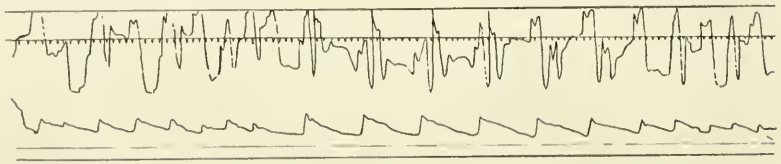
Hewlett and Barringer[10] report a case where there was dissociation of the action of the auricle and ventricle, the latter beating at a faster rate. The ventricular rate is twice as rapid (for periods) as the auricular in many cases of coupled beat action, but I have never seen dissociation accompanying this condition, such as they describe.

Conclusions. 1. Toxic effects of digitalis and related bodies may be divided into three periods with regard to their occurrence and severity. These toxic symptoms may usually be discovered in their earliest stages by careful and frequent sphygmographic observations. (1) Period of vagus stimulation; (2) period of depression

Tracing 17 (T. G., January 12, 1910).—Intraventricular heart block. Upper tracing a cardiogram taken at the left border of the sternum, fourth space. Lower radial. Heart markedly dilated. At *A* and *B* strong contractions occur at the right side, which are entirely absent or of insufficient force to open the valves of the left.



Tracing 18 (D. C., November 3, 1909).—Upper jugular, lower radial. Coupled beat phenomenon. The first contraction is not well defined, because the lever moved above the tracing paper.



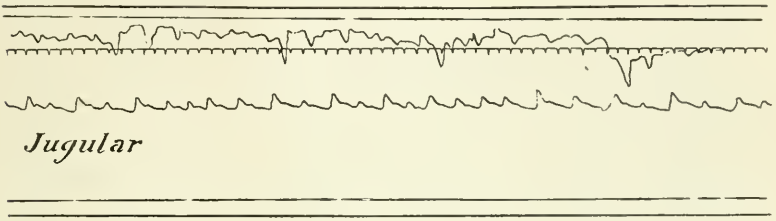
Tracing 19.—Same patient seven days later. No digitalis in the meantime. Phasic changes with coupled beat action evident in latter part of the tracing.

of conductivity with masked vagus action; (3) period of marked muscular irritability with depression of contractility.

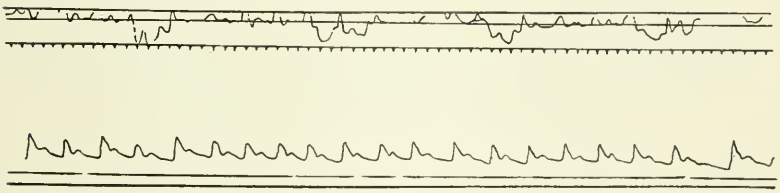
2. Digitalis heart block may be differentiated from ordinary heart block and from vagus influence as a causative factor.

3. Muscular irritability may be the first symptom observed, the other stages being short in duration and easily overlooked.

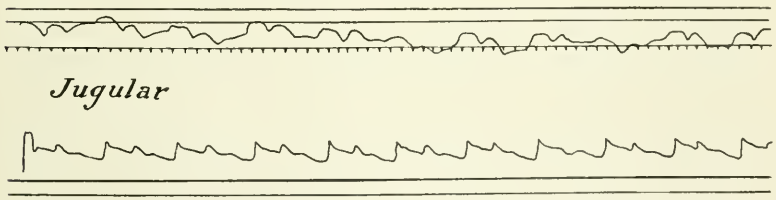
4. Irritability from digitalis must be differentiated from the progress of the disease by careful observations of the different functions as evidenced by combined tracings.



Tracing 20 (G., March 26, 1910).—Pulsus alternans before treatment.



Tracing 21.—From same patient two days later and after strophanthin treatment. In the beginning of the tracing a tendency to alternation may be seen.



Tracing 22 (C. C., April 12, 1909).—False pulsus alternans, coupled beat phenomenon with rapid pulse. Complete loss of compensation.

5. With therapeutic doses the rise of blood pressure due to vasoconstriction is so slight that it may be disregarded, but with toxic doses it becomes of extreme importance.

6. Cumulation occurs with digitalis and may last for a considerable period.

7. Vomiting is probably a central effect of digitalis and is a sign that absorption is occurring.

8. Pulsus alternans may be relieved by digitalis in some cases.

In taking the tracings the sphygmograph was so adjusted that the upper and lower levers would write on the same perpendicular line.

There are three tracings in this paper which did not come from patients in the Second Division of Bellevue. One was from Dr. C. N. B. Camac's service at the City Hospital and two from Dr. Alex. Lambert's service at Bellevue. I wish to express my appreciation to Drs. W. Gilman Thompson and Warren Coleman for the use and the privilege of reporting cases from their wards.

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PATHOLOGICAL AND EXPERIMENTAL DATA DERIVED FROM A FURTHER STUDY OF AN ACUTE INFECTIOUS DISEASE OF UNKNOWN ORIGIN.

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The opportunity to supplement the clinical study of an acute infectious disease of unknown origin, which was published in the Amer. Jour. Med. Sci. for April, 1910, has recently been given by my observation of a fatal case of the disease. This case opened the way to supply the lacking necessary pathological data which would carry the study nearer completion, and at the same time to furnish additional evidence that the disease has no relationship with any of the typhoidal group infections. A solution of the mystery, of what the disease really is, is no nearer completion than before.

From the experimental work which was carried on by inoculating blood obtained from patients with this disease into monkeys, details of which will be reported in this communication, it would appear that the relation of this disease to typhus fever is farther than ever from being indubitably established.

During the year ending December 1, 1910, we have observed and studied 34 additional cases, making in all 255 instances of the disease. Nothing obtained from the study of these later cases can

throw any added clinical light on the subject. There were no additional facts elicited which would change the picture of the disease already fully described.

For the benefit of those who may have no access to the original publication containing the description of this acute infectious disease, I would recall briefly its salient features. It begins rather suddenly, often by a distinct chill or chilly sensation. This is followed by general body pains and a headache of increasing agonizing severity. Fever develops quickly, the temperature reaching its maximum on the third day, after which it remains fairly constant, averaging between 103° and 104°, occasionally as high as 106°.

The patients are much prostrated, and in some, apathy is a prominent feature. On the fifth or sixth day of the disease an eruption appears, which is rather characteristic, and differentiates the disease from most other infectious diseases. The eruption is fairly profuse, but discrete, consisting of a maculopapular rash, dull red in color, erythematous in character; the spots are irregular in outline, though usually ovoid, 2 to 4 mm. in diameter. Under pressure a spot may be caused to fade, but it cannot be obliterated, thus showing an evident escape of some of the blood contents of the capillaries into the surrounding dermal tissues. Sometimes the spots become distinctly hemorrhagic (petechiæ). They appear on the trunk and extremities, even rarely on the palms and soles. The eruption is never as profuse as in measles, sometimes even being scanty, then showing less than one hundred individual spots, which may be fairly well scattered over the trunk, arms, and buttocks, and along the sides of the thighs. The eruption is permanent until the end of the disease; it does not appear in crops, but develops and reaches its full efflorescence within twenty-four hours after the first spots appear.

The disease lasts twelve to fourteen days, when the fever suddenly declines, in many cases with a critical fall in temperature, which may come to normal within twelve hours; in others, with a rapid lysis within thirty-six hours, and in a few, with lysis extending over a period of sixty hours. With the fall in temperature the agonizing headache disappears, the spots rapidly fade, leaving within a few hours only brownish-yellow stains on the skin, sometimes disappearing altogether within twenty-four hours thereafter. Convalescence is speedy. In a few cases rigidity of the neck and Kernig's phenomena appear. The urine in most cases shows a trace of albumin and hyalogranular casts. The white blood count averages 11,000 cells. The blood shows no power of agglutinating any of the organisms of the typhoidal group. Blood cultures are absolutely negative.

The disease has never been spread to anybody in the wards of the hospital nor to any of the hospital personnel, nor have I observed it in more than one member of a family, with one exception.

The description of the disease was based on a previous experience, with 221 cases. During the last year we have had more admissions of the disease to the wards in Mount Sinai Hospital than in any previous year. From December 1, 1909, to December 1, 1910, 34 patients with this disease were admitted.

A study of these 34 cases following the method of reporting the preceding 50 cases of the 221 cases shows the following statistical facts:

Sex. There were 17 males and 17 females.

Age. The youngest patient was eighteen years of age, the eldest was fifty-nine. Two cases occurred in the second, 14 in the third, 5 in the fourth, 7 in the fifth, and 6 in the sixth decades.

Nativity. Bearing in mind former reference to the preponderating number of Russians who are patients at Mount Sinai Hospital, the nativity of the most of these cases is Russian; of this group 27 were born in Russia, 5 in Austria, 1 in Hungary, and 1 in Italy.

Month of Appearance. Two cases entered the hospital in January, 1 in February, 5 in March, 4 in April, 3 in May, 1 in June, 2 in July, 2 in August, 3 in September, 4 in October, 4 in November, and 3 in December.

In this group then it would appear that there were two periods of activity of the disease in the last year: (1) In the spring, and (2) in the fall, the first half of the year showing fewer cases than the second half. This is in accord with our study of the preceding cases. The last 50 of the preceding 221 cases showed 18 in the first half and 32 in the second half of the year.

Previous Typhoid. Ten previously had had typhoid fever, 20 had not, and in 4 the question of previous typhoid infection could not be ascertained.

Onset. In 16 cases the disease began suddenly without premonitory symptoms; in 18 cases the onset was gradual. Of the latter there were 8 cases in which no definite data of onset could be obtained, probably because the disease developed insidiously. In 2 cases there was a prodromal stage of two days, in 2 of three days, in 2 of four days, in 2 of five days, in 1 of six days, and in 1 of seven days before a pyrexia developed.

Contagion. A much more searching inquiry was made in these cases as to any other member of the family being ill with this or with a similar disease, and whether any other individual in the same abode had a febrile disease. The result was entirely negative.

Class of Patients. I have seen but two instances of the disease in the higher classes of society; all the other cases were in hospital patients, hence in people of the poor or pauper classes. A careful search of the skin for evidence of bites of pediculi or bites of insects in these cases gave mostly negative results.

Duration. In this series the shortest duration of the disease was ten days, of which there were 2 instances; the longest nineteen

days, also 2 instances. Between ten days and fifteen days there were 29 cases, and between fifteen and nineteen days, 5 cases. The average duration of the fever in this group was 13.7 days.

Termination. Using the same terms as in the previous communication, we find that 16 of these cases ended their disease suddenly by crisis, 4 terminated by rapid lysis, 13 by lysis, and 1 in death on the tenth day of the illness.

It was this fatal case which will, I believe, contribute important facts to our knowledge, and for that reason will justify the report of a short abstract of the clinical history.

Case I.—Lena T., female, aged forty years, born in Russia, was admitted to my service at Mount Sinai Hospital October 28, 1910.

The history of her illness showed that it began five days before that date, suddenly, with a chill, vomiting, and headache, which were rapidly followed by fever. She had to take to bed immediately, as she felt prostrated, and generally sick. The headache increased, with intensifying violence, affecting the entire frontal and both temporal regions. She had no epistaxis, no cough, and she did not notice any eruption.

She definitely stated that no other member of her family was similarly ill, and she knows of nobody in the house who was sick at the time. Inquiry into her previous condition showed that she had typhoid fever in her fifteenth year. She gave no history of symptoms on inquiry which would suggest the presence of any previous cardiac, renal, pulmonary, or gastric disease.

Physical Examination. The patient is well built, of average height, of well-developed musculature, and is well nourished. She lies in bed in condition of relaxation, with contracted brows, and moans with pain, which is confined to her head. She gives the appearance of listlessness and apathy, and is apparently considerably prostrated.

The head is fixed, and shows rigidity of the neck when attempt is made to flex it on the chest. The eyes are suffused, the conjunctivæ congested, the pupils equal, regular, central, somewhat contracted, and react equally to light and to accommodation. There are no ocular palsies. No petechiæ can be found on the conjunctivæ. The lips are pale, teeth mostly artificial, gums atrophied, tongue dried and coated with white fur, excepting tips and sides.

The nose, ears, mastoids, larynx, trachea, and thyroid gland present no apparent evidence of abnormalities.

The skin is of the brunette type, and presents a maculopapular eruption, everywhere discrete, situated over the upper abdomen, over the flanks extending to the hips, and upward into the axilla. The extremities are free from eruption, excepting a few spots, six, on the left upper arm. The size of the spots varies from a pinhead to 4 mm. The eruption is slightly raised, and dull red in color,

irregular in outline, and the spots fade without disappearing on pressure. There are no palpable lymph nodes.

The chest is markedly funnel-shaped, the expansion is poor, and breathing is slow. Anteriorly on auscultation the respiratory murmur is feeble and somewhat distant; a few scattered mucous rales are heard, especially posteriorly, where the breath sounds are of the same character as in front. At both apices there is marked dulness, diminished breathing, prolonged high-pitched expiration (healed tuberculosis?).

The heart shows no enlargement of its borders; the apex is neither visible nor palpable. The sounds are best heard in the fifth interspace in the midclavicular line; they are of good quality, the second being accentuated.

The pulses are equal, regular, slow, dicrotic, and apparently of normal tension.

The liver is not palpable; dulness begins at the fourth rib, flatness at the sixth, and extends to the free costal border.

The spleen is not palpable, its upper border being apparently at the seventh rib.

The abdomen is slightly distended, there being neither local tenderness nor rigidity, and presents the rash just described.

The extremities show nothing abnormal. The knee-jerks are equal, slightly increased, and Achilles tendon reflexes are elicited readily. There is no Kernig symptom.

Vaginal examination shows a cystocele and a lacerated cervix; the fundus uteri is apparently normal.

Rectal examination reveals nothing abnormal.

The white blood count made after admission was as follows: White blood cells, 16,000; polymorphonuclears, 90 per cent.; large lymphocytes, 6 per cent.; small lymphocytes, 3 per cent.; large mononuclears, 1 per cent.

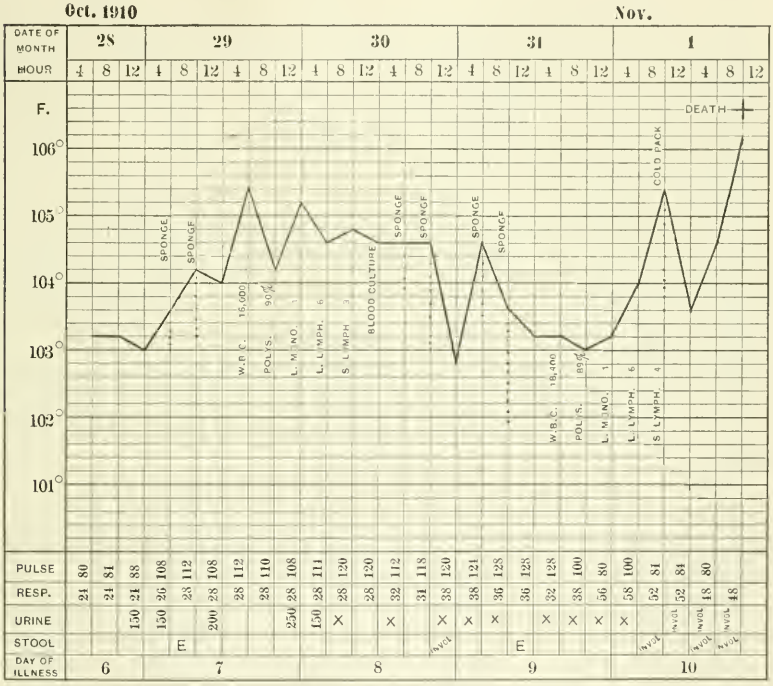
Two days later, October 31, being the day before her exitus, the blood count showed the white cells to be 18,400; polymorphonuclears, 89 per cent.; large lymphocytes, 1 per cent.; small lymphocytes, 6 per cent., and large mononuclears, 1 per cent., practically no change developing from the count of two days before.

The urine showed evidences of a chronic nephritis; specific gravity, 1028; acid; cloudy; and contained a heavy trace of albumin and a number of granular casts. Daily examination showed the same amount of albumin and casts.

October 29, 1910. Today the patient is more markedly prostrated, and is getting stuporous. The rash has extended so as to involve the trunk anteriorly and posteriorly as well as the extremities down to and including the fingers and toes, especially on the extensor surfaces; two spots are seen on the right palm, three on the left; on the plantar surface of the left foot near the outside, two spots are noted. An ocular examination made today reveals

no abnormality of the fundus. Rigidity of the neck is more marked. The pulse remains of fair quality, is rapid, average number of beats, 116, and regular. Blood pressure, 110, systolic.

October 30, 1910. The rash seems to have reached its full development. It is found distributed over the same areas as in yesterday's note, and no new spots seem to have appeared. There is a marked change in the quality of the heart sounds, which are getting poor, especially the first sound. The pulse shows a tendency to irregularity, otherwise the condition is the same as in yesterday's note.



Temperature chart of the patient; fatal termination.

October 31, 1910. The patient seems to have lost considerably in strength, the stuporous condition is very marked, and it is only with great difficulty that she can be aroused. Her position is one of extreme relaxation; she lies motionless, excepting for a picking of the bedclothes. Her respirations are deeper, more rapid. She appears "toxic" in the extreme. The pulse is rapid, feeble, and with an irregularity very pronounced; the heart sounds are so indistinct at times as to be almost inaudible, the heart rhythm being irregular. Some of the old spots have become darker in color, and a few are distinctly hemorrhagic or petechial; two petechiæ are noted in

each conjunctiva. There have been involuntary evacuations both from the bowel and bladder. Kernig's phenomenon was elicited today; the neck is still rigid.

November 1, 1910. This morning the patient's condition is as poor as it can be. She shows at times a wandering muttering delirium, and she is only semiconscious. The heart action is very poor, the pulse weak, and very irregular. She has involuntary urination and defecation. The temperature, which has persisted between 103° and 105° since her admission, shows no tendency to break. The eruption is slightly fainter than yesterday and looks as if it were beginning to fade. Active cardiac stimulation is ordered, as the patient's condition seems precarious. This afternoon, at five o'clock, the heart action is rapidly diminishing, the pulse is at times imperceptible, and stimulation has had no effect.

Death came on rapidly at 7.45 P.M., from insufficiency of the heart muscle induced by the toxemia of the disease.

A blood culture was taken on the seventh day of her disease, with negative results.

Daily examinations for agglutination against the typhoid organisms were made, likewise with negative results. The above temperature chart shows the course of her fever throughout the period of observation.

For the following report of the autopsy, the pathological and the bacteriological findings, I am indebted to the pathological department, Dr. F. S. Mandlebaum, director, and his staff, to whom I here express my appreciation of their work, together with my thanks.

Protocol. Microscopic examination and bacteriology of autopsy. Lena T., aged forty-five years. No. 118547. Died November 1, 1910, at 7.45 P.M. Autopsy 2000, performed by Dr. E. Libman and Dr. Alfred E. Cohn, November 2, 1910, at 1.30 P.M.

General. Body of a well-nourished female, 160 cm. long. The bony development is good; there is marked rigor mortis. Two small fading petechiæ are seen in the conjunctiva of the upper lid of the left eye; there are also a large number in the conjunctiva of the lower lid of the right eye. Numerous petechiæ are scattered over the skin of the trunk anteriorly and posteriorly, and a few on the upper part of both thighs, arms, and forearms.

Mammary Glands: Negative.

Abdomen: The musculature of the abdominal wall is deep red in color. The diaphragm on the left side is at the fourth space, on the right side at the fourth rib. There are a few fine adhesions between the anterior surface of the liver and the abdominal wall. The muscles are fairly deep red in color. There are adhesions of the gall-bladder to the transverse colon.

Thyroid: There is slight parenchymatous degeneration.

Chest: There is no fluid in either pleural cavity. There are firm

adhesions over the right lower lobe. About 5 c.c. of fluid are found in the pericardial sac. There are firm adhesions at the left apex.

Right Lung: There is puckering at the right apex; firm, old fibrous bands at the lower right lobe. Interlobular fissures are smooth. The general color is grayish blue with anthracotic mottling; the anterior border is lighter gray and the surface is irregular, due to bullæ of emphysema. On section the color is dark bluish, brownish red. Fluid blood oozes from the cut surface. There is neither edema nor consolidation. The pulmonary artery contains postmortem blood clots, there is slight atheroma of the main branches. The bronchial lymph nodes show marked anthracosis, but no enlargement and no tuberculosis. Bronchi show marked congestion of the mucous membrane. There are no retained secretions.

Left Lung: There is marked puckering at the apex and some retraction. On the surface of the retracted areas there are dense fibrous adhesions. The surface is smooth, the color and distribution of the emphysema similar to the right side. There is a rudimentary upper incisure. On section the color, edema, and surface appearance are like on the right side. There is marked congestion, emphysema, but no consolidation. The apex portion shows marked anthracosis. There is marked irregularity of the cut surface, showing a few cheesy and calcified areas. A few not dense connective-tissue strands pass through this area. The pulmonary artery is normal. The bronchi are congested, as on the right side. The bronchial lymph nodes are not enlarged; they show marked anthracosis, but no tuberculosis.

Heart: The heart is normal in size. Along the postventricular groove it measures 9 cm., along the anterior interventricular groove 11 cm. The pericardium is smooth. There is very marked fatty overgrowth over the right ventricle, a little over the left, both on the anterior and posterior surfaces and at the apex. The right auricle contains fluid blood. The endocardium of the auricle is thin, translucent, and shows a moderate amount of subendocardial fat. There is a marked Chiati net. There is some dilatation, but no hypertrophy. The tricuspid valve admits more than three fingers; circumference is 12.5 cm. The cusps of the valve show thickening above the free border to the extent of 5 mm. There is no recent lesion and puckering. Conus arteriosus is slightly dilated, muscle being very flabby, and showing a moderate fatty ingrowth; there is atophy, but no hypertrophy. The muscle is markedly brown. In the right ventricle there are a few red clots. Scattered through the ventricle are a number of small, irregular, yellowish areas. Cusps of the pulmonary artery show bloody imbibition. In the left auricle the endocardium is markedly thickened. The mitral valve admits three fingers; the circumference of the open

ring is 9.6 cm. There is marked thickening of the free edges of the valve, the character of the thickening being like that of the tricuspid valve. There is fairly marked dilatation of the outflow tract. The conduction system is easy discernible. The left ventricle measures 9 cm. at the base, 14 cm. at the mid-level, and 10 cm. at the apex. The color is like that on the right side. The aortic valve shows slight thickening of the lunulæ at the attached margins. There is atheroma at the root and in the descending aorta. There are thickened and sclerotic patches at the ductus Botalli. The atheroma reaches into the innominate, right subclavian, and right carotid arteries. The muscle shows marked parenchymatous degeneration. The coronary arteries show slight atheroma. The foramen ovale is closed. The weight of the heart is 341 grams. The inferior cava is normal. Abdominal aorta shows slight atheroma.

Intestines: The duodenum is bile-stained and hyperemic. The congestion continues throughout the gut. The mesenteric nodes are not enlarged. Neither lymph follicles nor Peyer's patches are enlarged. Near the ileocecal junction there is a calcareous cheesy gland about the size of a bean. The suprapancreatic lymph nodes are calcareous.

Liver: Somewhat enlarged. Exceedingly flabby. The peritoneal surface is smooth; the color is dirty pinkish brown. On section it is soft and flabby. The lobules are distinct, the centres depressed and red; there is slight fatty degeneration. The color on section is brownish-red. In the liver there are irregular areas 2 to 3 cm. in diameter, more fatty and yellow than the rest. The weight is 1922 grams, including the gall-bladder.

Gall-bladder: Contains thick dark green bile. One mulberry stone, 2 x 2.5 cm., is found in the gall-bladder.

Stomach: Contains about 100 c.c. of dark grayish-green fluid material. The mucous membrane shows marked postmortem digestion. Near the fundus there are submucous hemorrhages.

Pancreas: Normal in size, pinkish gray in color, and flabby.

There is marked parenchymatous degeneration and slight congestion. The weight is 124 grams.

Spleen: Normal in size. It measures 13 x 8 x 3.5 cm. The surface is smooth, the color is bluish gray. On section it is moderately soft, and the trabeculæ are markedly prominent. There is hyperplasia of the lymph follicles. The splenic pulp is congested and shows a number of small hemorrhages. The pulp scrapes moderately easily. The weight is 155 grams.

Kidneys: Right—The capsule is not adherent except at the entrance of the capsular vessels, of which there are a considerable number. There is fetal lobulation. At the external border there are a number of scars, but the surface is otherwise smooth. The kidney is large, and the hilus is unusually large. On section there is moderate congestion. The markings of the cortex are distinct

except at points, where there are surface scars. The pelvis shows no abnormality. The organ measures 14.5 x 7 x 3 cm. Left—The capsule, surface, and scars are similar to those on the right side. The organ measures 12.5 x 5.5 x 3 cm. The weight of both together is 403 grams.

Adrenals: Both of normal size. There are no extracortical adenomas. The zona pigmentosa is poorly marked, and for the most part is in entire-solution; the medulla is normal in amount, but poorly stained.

Urinary Bladder: Markedly dilated, and is large enough to hold three fists; it is not trabeculated.

Uterus: Measures 9 x 4 x 2 cm. There is apoplexy of the body.

Ovaries: Show no abnormality.

Tubes: There is a small cyst at the fimbriated end of the right tube.

Bone Marrow: The femora only were opened. The color of the marrow for the most part was grayish yellow, but there were irregular streaks and additional small areas which were raspberry red. The entire section gives the impression of disseminated congestion.

Microscopic. Heart is markedly congested; there is moderate bipolar pigmentation and slight parenchymatous degeneration; no fragmentation; no fatty degeneration. There is moderate fatty ingrowth.

Lung: There is marked congestion, anthracosis, and emphysema. Another section shows still more marked congestion, with slight edema and a few areas in which there is a growth of dense fibrous tissue surrounded by additional fibrous tissue containing a few more fibroblasts and lymphocytes. These areas are intensely anthracotic. Giant cells are not seen.

Liver: The capsule is normal. There is marked congestion, showing markedly increased numbers of lymphocytes and fibroblasts in Glisson's capsule. There are areas of congestion so marked that they have the appearance of being hemorrhagic. A few areas are seen in which the liver cells have lost their character, and in which there are collections of lymphocytes (focal necrosis). About the central veins there are rarely found collections of lymphocytes; there is also central pigmentation. There is practically no fat degeneration.

Spleen: Shows well-developed Malpighian bodies, which are slightly hyperplastic. There are numerous diffuse but small interstitial hemorrhages.

Pancreas: Congested, but shows no other lesion.

Kidney: Marked congestion, parenchymatous degeneration, occasional subcapsular collections of round cells (lymphocytes and plasma cells). An occasional glomerulus has undergone fibrous degeneration.

Adrenals: Congested. There is solution in the zona pigmentosa. The medulla is well preserved and contains an occasional round cell.

Uterus: Areas of interstitial hyaline degeneration.

Ovary: No abnormality.

Thyroid: Shows in one portion a small area of adenomatous hyperplasia.

Bone Marrow: Shows the greater part to be fatty; the vessels are everywhere markedly congested. There are evidences of hematopoiesis, inasmuch as there are bone-marrow giant cells, erythroblasts, myeloblasts, and myelocytes.

Anatomical Diagnosis. Adenoma of thyroid; brown atrophy and parenchymatous degeneration of the heart; calcareous nodules at the apices of the lungs; congestion, anthracosis, edema, insular fibrosis of the lung; congestion, focal necrosis (?), inflammation of Glisson's capsule in the liver; hemorrhages in the spleen; congestion; parenchymatous degeneration of the kidneys; solution in the zona pigmentosa of the adrenals; calcareous ileocecal lymph nodes.

Bacteriology. By Dr. E. P. Bernstein and Dr. H. L. Celler.

Cultures: From the blood of the heart show: (1) Staphylococcus citreus, (2) Sarcina lutea, (3) chromogenic Gram-positive bacillus, not identified.

Cultures from the Bile: (1) Bacterium coli, (2) Staphylococcus citreus, (3) Gram-positive bacillus, long, with rounded ends occurring in chains of two and three, not identified.

Cultures from the Spleen: (1) Staphylococcus albus, and (2) Gram-negative bacillus, with pointed ends.

Growth characteristics of the bacillus:

Agar: Heavy, moist, slimy growth.

Medium 1: Yellow, slimy growth; no precipitation.

Potato: Heavy, yellowish-brown growth.

Milk: Acid, coagulation (two days).

Gelatin: Not fluidified.

Indol: Negative.

Bouillon: Diffusely cloudy.

Fermentation Tubes:

Glucose: Heavy growth in bulb only, alkaline (four days).

Saccharose: Heavy growth in bulb only, alkaline.

Lactose: Heavy growth in bulb only, alkaline.

Mannit: Heavy growth in bulb only, alkaline.

Two guinea-pigs were injected, one with spleen pulp and the other with liver pulp.

Guinea-pig No. 688: Spleen—Gram-positive bacillus unidentified. Staphylococcus albus.

Guinea-pig No. 689: Liver—Gram-positive bacillus. Staphylococcus albus.

From this report the conclusions may be reached that the organs showed congestion and general parenchymatous degeneration such as would obtain in any intense infectious disease. It is noteworthy, in consideration of the fact that many believe this disease to belong to the typhoidal-group infections, that the intestines showed none of the lesions which are characteristic of typhoid fever. The presence of Staphylococcus albus and citreus and the unidentified bacilli were most probably due to agonal or postmortem invasion, and were non-pathogenic.

The appearance of the patient on the last day of her illness, with the clinical picture of coma, petechial eruption, carphology, paralysis of the sphincters, and the rapid elimination of the heart action, recalled to my mind two other fatal cases on my hospital service with a similar picture, one occurring in March, 1902, and one in May, 1903, the former a female, the latter a male. Both of these patients were brought to the hospital in stupor, and were diagnosticated by me as typhus fever. These were the only instances of a similar or identical disease in which coma and a fatal outcome were noted. On this account I could not reconcile them with the picture of the disease, which I had constructed from previous experience. They were both reported as possible typhus fever to the health authorities, from whom permission for autopsy was obtained. I had previously excluded them from a place in this group on account of the intensity and virulence of the symptoms. Had I seen them earlier in the course of their infection perhaps they would have been included and been reported as the first fatal instances of this disease. The clinical histories of these cases in brief were as follows:

Case II.—Alte F., female, aged thirty-seven years; midwife; born in Austria. Hospital No. 71259. Admitted to my service March 2, 1902.

Her illness began ten days before, with general malaise, pain in the back, limbs, and severe headache. Three days later patient went to bed. After this she had repeated chills, high fever, but without sweats. There has been vomiting since onset, and follows immediately after ingestion of food. Headache is intense. There has been no delirium. Four days before admission (sixth day of illness) an eruption appeared on body and extremities.

Physical Examination. Well nourished. Tongue dry and coated. No palpable lymph nodes. Conjunctiva injected. Pupils contracted. Face flushed. Respirations rapid, somewhat labored. Patient in constant restlessness, attempts to leave bed. No tremor. All over her body and extremities there is an eruption, partly petechial, partly erythematous, dull red, consisting of macules and papules, closely set together, but discrete. There are a few vesicles on right forearm, surmounting petechial bases.

Lungs: Vesicular murmurs; subcrepitant rales at both bases.

Heart: Sounds distant and feeble; slight accentuation of second pulmonic. Apex beat indistinguishable.

Pulse: Full, strong, and regular.

Liver: Dull at fourth space, flat at sixth rib. Lower border not palpable, owing to rigidity of rectus.

Spleen: Palpable 1 cm. below free costal edge.

Extremities: No eruption below knees.

March 3. Patient is delirious. No change in eruption.

March 4. General condition worse. Marked tremor of hands Heart sounds feebler. Eruption beginning to fade. With increasing delirium, stupor, and cyanosis, on March 7 had a hemorrhage of about 15 c.c. from uterus; the patient sank into coma, and death occurred the following day, at 4.50 P.M.

The urine showed albumin, a positive Ehrlich, and contained hyalogranular casts.

Widals on March 5, March 6, and March 7 were negative—1 in 20 and 1 in 50. Her temperature varied between 106° and 106.6° without much excursion; pulse between 116 and 130; respirations, 28 to 42.

Protocol. Microscopic Examination and Bacteriology of Autopsy No. 840. Alte F., aged thirty-seven years. No. 71259. Died March 8, 1902, at 4.50 A.M. Autopsy performed by Dr. E. Libman, March 9, 1902 (twenty-nine and one-half hours post mortem).

General. Marked rigor mortis of the lower extremities. Fading papular rash over the trunk anteriorly and posteriorly. Muscles are pale.

Lungs: Marked adhesions of the right upper lobe. Both lower lobes are very firm and intensely congested. The rest of the lungs are modertely congested. There is marked edema of the lungs. The bronchial nodes are enlarged.

Esophagus: Shows moderate varicosities of veins.

Heart: The heart is flabby. The veins on the surface are somewhat tortuous. Right auricle moderately dilated. Fatty overgrowth of right ventricle and infiltration of the wall; the ventricle is moderately dilated, and contains a fat clot. The wall is thin, the muscle pale, and the valves negative. Pulmonary artery negative. Left ventricle moderately dilated; the walls are thin. The mitral valve is slightly thickened. Aortic valve negative. Endocardium whitened. Heart muscle pale and cloudy; appears fatty. Coronary arteries are negative.

Trachea: Mucosa reddened and swollen, and contains blood.

Spleen: Much enlarged, flabby, and soft. On section the pulp is congested, soft, almost diffluent. A number of hemorrhages are present.

Liver: Moderately enlarged and flabby. On section it is cloudy and appears fatty.

Kidneys: *Right*—Flabby, but normal in size. The surface is

congested. The capsule is not adherent. On section the cortex is swollen; there are markings of congestion. The color is grayish. There are three small nodules in the pyramids; one about $\frac{1}{3}$ cm. in diameter; the others are the size of the head of a pin, white in color and firm (fibromata). *Left*—This is the same as the right, except that the capsule is more adherent, and there are two small cysts on the surface.

Adrenals: Negative.

Bladder: Small and contracted. There is marked injection of veins and capillaries of the mucosa.

Uterus: The mucosa is reddened and elevated at the fundus. The muscle is soft. Tubes are negative.

Ovaries: The ovaries are firm and fibrous. In the right ovary there is the scar of a corpus luteum.

Stomach: There are a few hemorrhages near the pylorus.

Intestines: Negative. The Peyer's patches are not enlarged, but rather depressed. Solitary nodules just apparent.

Vena Cava: Inferior mesenteric and iliac and portal veins negative.

Pancreas: Negative.

Brain: Practically negative. The vessels are injected. Mastoid processes and accessory sinuses are negative.

Bacteriology. Cultures made from heart blood and spleen (by puncture) fifteen hours post mortem showed the Staphylococcus albus (anaërobic studies were also made). Heart blood, 10 c.c.; 5 c.c. in plates; 5 c.c. in flasks; some aërobically, some anaërobically. Staphylococcus albus.

Stool (from lower ileum): No typhoid bacilli found.

Microscopic Examination.

Heart: Acute inflammation, brown atrophy, and fragmentation.

Liver: Cloudy swelling and fatty degeneration.

Spleen: Acute splenitis and congestion.

Pancreas: Acute changes.

Kidney: Marked acute degeneration and congestion.

Uterus: Wall negative.

Case III.—Kalman, R. Hospital No. 75752. Admitted May 26, 1903. Patient's illness is of six days' duration, beginning suddenly, with headache and pain in back and left abdomen, followed very quickly by a chill, abdominal pain, and headache of increasing severity. Did not notice any eruption. Abdominal pain disappeared on the third day. Fever prominent.

Physical examination revealed conditions similar to previous case. The eruption covered the entire body, was entirely of dull red, erythematous maculopapules. It was not on neck, fingers, palms, or soles.

Patient is somnolent and stuporous.

Spleen is palpable.

Blood count: White blood corpuscles, 7000.

May 28. White blood corpuscles, 11,000.

May 29. Face becoming dusky; lungs show evidence of congestion; spleen, 1 cm. larger than on May 27. Patient delirious.

May 30. Eruption much darker, now distinctly petechial on arms; face more dusky, lips cyanotic. Coma vigil very marked. Abdomen distended. Slight rigidity of neck. Pulse much weaker. Heart sounds very faint, with increasing general cyanosis. Exitus at 11 P.M.

Urine: Acid, 1010 to 1016. Heavy traces of albumin and hyaline and granular casts. Positive Ehrlich.

Temperature: Excursions from 104° to 104.8°.

Respirations: 26 to 36.

Pulse: 120 to 136.

Protocol. Bacteriology and Microscopic Examination of Autopsy No. 953.

Kalman, R., aged thirty-two years. No. 75752. Died May 30, 1903, at 11 P.M. Autopsy performed by Dr. G. P. Biggs, of the Health Department, May 31, 1903, seventeen hours after death.

General. Moderate rigor mortis. Numerous petechiæ on the trunk and extremities. Over the upper surface of the first phalanx of the left big toe there is a superficial wound almost healed.

Lungs: Both are congested and edematous, the upper lobes more markedly so. The lower lobe on the right side shows a partial subdivision. There are numerous subpleural hemorrhages. The bronchial nodes are slightly enlarged and anthracotic.

Heart: The mitral flaps are thickened. The heart muscle is pale. The blood is very fluid in character. The aorta and the coronary arteries are negative. There are no petechiæ on the pericardium.

Liver: The whole liver is soft and yellow. The right lobe is fatty and degenerated in appearance, and friable. The left lobe shows similar changes, but they are much less marked. The lobules are not distinctly marked. There are small hemorrhages in the right lobe (intralobular). There is intense acute degeneration, with necrosis.

Spleen: Enlarged. The capsule is slightly wrinkled. The pulp is dark and soft, almost diffluent in the central part.

Stomach: Negative. The stomach contents are thick, dark, semifluid.

Intestines: Negative. There is no enlargement of the retroperitoneal lymph nodes. On the mesentery there is a hemorrhagic area 1.5 cm. in diameter.

Pancreas: Dark in color and of a rather soft consistency (postmortem change?).

Kidneys: The left kidney is enlarged, and shows acute nephritis. There are some petechiæ on the pelvis. The right kidney is smaller

than the left, and shows acute nephritis. There are some petechiæ in the pelvis. The markings are indistinct. There are a few cortical hemorrhages.

Bladder: The urine is clear. Situated in the median line at about the apex of the trigonum there are two hard, small, dark bodies, which are freely movable and project into the interior of the bladder. They are somewhat smaller than beads.

Brain: The dura mater is negative. The pia is slightly cloudy and the vessels somewhat congested. The brain is otherwise negative.

Bacteriology. Cultures from heart's blood and spleen, Bacterium coli.

Microscopic Examination.

Heart: Brown atrophy and chronic inflammation.

Mitral Valve: Chronic inflammation.

Liver: Focal necrosis, acute degeneration, fatty degeneration, regeneration, and acute hemorrhage.

Kidney: Acute nephritis.

Spleen: Acute inflammation.

Pancreas: Acute degeneration.

Bladder: Calculus in the wall.

Experimental. In the endeavor to determine whether this disease bore any relation to typhus fever, an attempt was made to imitate some of the work of Nicolle, Anderson and Goldberger, and Ricketts and Wilder in their experimental studies on typhus fever. All of these investigators were enabled to produce typhus fever experimentally by inoculating into monkeys the blood of human subjects who were suffering from that disease. There were some differences in their results, which ought to be mentioned.

Nicolle,[1] and his associates Comte and Conseil were the first in this experimental field. They met with failure in their first attempt to inoculate two monkeys, Macacus sinicus, with the blood of human typhus subjects. He (Nicolle) then conceived the idea of using an anthropoid for the experiment, and succeeded in inoculating typhus fever into a chimpanzee with blood from the same patient with which he tried to transmit typhus into the macacus. The chimpanzee died as the result of the fever. During its illness its blood was inoculated into another monkey, Macacus sinicus, and produced a typical attack of typhus fever. The blood, however, taken from this macacus proved infective for the Macacus sinicus only and for no other varieties of macacus tried.

Inoculation of the human typhus blood into the first two macaci of the series apparently produced an immunity in them to the disease, though it did not induce the disease. This was proved by the fact that these monkeys were not susceptible to a subsequent

[1] Ann. de l'Inst. Pasteur, 1909, xxiv, 243.

inoculation of blood taken from the monkeys who were suffering from experimental typhus.

Nicolle was able to transfer the disease to macacus monkeys through the bites of body lice which had fed on the typhus infected chimpanzee. He showed that the typhus of Tunis, where the investigations were carried on, was most likely conveyed by bites of infected body lice and not by fleas or bedbugs.

Anderson and Goldberger,[2] in their inquiry into the relationship of Rocky Mountain spotted fever, or tick fever of Montana to typhus fever, devoted much time to the study of typhus fever as it existed in Mexico City, where they carried out experimental studies on inoculation of typhus fever into monkeys, thus following Nicolle's work, and into guinea-pigs, rabbits, and rats. They readily succeeded by intraperitoneal inoculations of defibrinated human typhus blood directly into Macacus rhesus in producing typhus fever in this variety of monkey. Similar blood was also injected into a capuchin monkey (Cebus capuchinus), and the disease was likewise thereby produced. After their attack both these monkeys were immune to further inoculations.

Blood passed through a Berkefeld filter was unable to induce the disease.

These authors give good reasons to show that typhus may be communicable in man only through an intermediary host and not by contact. They advance evidence, as did Nicolle previously, to show that it is not the flea nor bedbug, but the body louse which may be the offending medium of transmission by their bites. They succeeded in transmitting the disease from man to monkey by means of lice, Pediculi vestimentorum, which were permitted to feed previously on human typhus patients. Their conclusions are important enough to warrant their being here recorded:

"1. At least two species of monkeys, Macacus rhesus and Cebus capuchinus, are susceptible to direct inoculation with the blood from human cases of Tabardillo (typhus fever, Mexican).

"2. One attack of the disease in the monkey produced by blood inoculation directly from man induces a definite immunity to a subsequent inoculation with virulent blood.

"3. The blood from human cases of tabardillo is infective on at least the eighth day of the disease. It seems probable, however, that it will be found infective throughout the active febrile stage of the disease.

"4. The blood from the monkey Macacus rhesus is infective by passage to a second monkey of the same species on at least the fifth and sixth days of the disease.

[2] Public Health Reports, Public Health and Marine Hospital Service, Treasury Department of United States, vol. xxiv, No. 50, p. 1861; No. 52, p. 1941; December 10 and December 24, 1909, and vol. xxv, No. 7, p. 177, February 18, 1910.

"5. Diluted blood serum from a human case of tabardillo, when passed through a Berkefeld filter, failed when inoculated into a monkey to produce the disease.

"6. The blood of a monkey of the species Macacus rhesus is infective, though its infectivity is attenuated to a second monkey of the same species.

"7. The disease is not conveyed by fomites as such, nor is it contagious in the ordinary sense of the word.

"8. The epidemiological facts of the disease, in our opinion, point unmistakably to an insect intermediary; and we believe that our observations point strongly to the body louse (Pediculus vestimenti) as this insect.

"9. We are of the opinion that the evidence against the body louse as the transmitter of tabardillo is sufficient to demand that prophylactic sanitary measures directed against this disease should take into consideration that insect."

The fact to be emphasized in the comparison of the results of the experimental studies of Nicolle and of Anderson and Goldberger are, (1) the inability of the former to transmit typhus fever directly from infective human blood to the macacus monkey, and (2) the success in this regard of the latter. This might seem to indicate a lack of identity or rather a difference in the typhus of Tunis (old world typhus) and that of Mexico City. Indeed, Goldberger and Anderson[3] call attention to the fact that Mexican physicians for many years have contended that the two forms of typhus are clinically dissimilar, the chief difference being in adults, at least, in the slower onset and slower defervescence of the Mexican disease. The second fact to be emphasized is the corroboration by our countrymen of Nicolle's theme that the disease may be transmitted through the bite of the typhus infected body louse.

Ricketts and Wilder[4] confirmed by similar experiments, also made in Mexico City, the susceptibility of the monkey to inoculations with the blood of patients suffering from the typhus fever of Mexico. They were successful in inducing the disease by a single injection (Anderson and Goldgerger had succeeded only with multiple injections) into a Macacus rhesus.

The symptoms which indicate typhus fever in the monkey are fairly constant and similar to those of man; there is an incubation of a somewhat uniform duration, a sudden onset of fever, decided illness, and rapid defervescence. The negative outcome of blood cultures and the more or less negative autopsy findings correspond fairly well with typhus fever in man.

Rickets and Wilder also proved experimentally that blood serum is as infective as defibrinated blood. They used diluted blood serum

[3] Public Health Reports, vol. xxv., No. 7, p. 184.

[4] The Typhus Fever of Mexico (Tabardillao, Jour. Amer. Med. Assoc., 1910, liv, No. 6, p. 463; No. 16, p. 1304; No. 17, p. 1373.

because they found in the experimental work with inoculations with Rocky Mountain spotted fever that dilution seemed to favor infection, and explained this by the fact that "dilution is known to render less effective specific antibodies which may be destructive to the virus," stating that "there can be little doubt that blood drawn from typhus patients on the eighth day of the disease contains germinal antibodies, particularly since the disease is one which, clinically, is known to cause the development of distinct immunity."

No eruption resembling that of typhus has been detected in the monkeys suffering from the inoculated disease.

These authors also confirmed Anderson and Goldberger's filtration experiments with typhus fever blood serum. It seems fairly well proved then that the virus of Mexican typhus belongs to the unfilterable.

Filtered human Mexican typhus serum cannot produce the experimental disease. A monkey which received the unfiltered serum exhibited a severe course of fever after an incubation period of five days, whereas an animal which received the filtered serum developed no fever and remained perfectly well.

Immunity tests were given to the animals who suffered with experimental disease after subsidence of the fever by a second inoculation of human typhus infected serum, and this failed to produce the disease. The immunity tests were controlled by the injection of a similar amount of the same blood serum into a normal (non-typhus infected) monkey, and the disease was produced. These authors also came to the conclusion that the epidemiological conditions are best explained by insect transmission, especially by the Pediculus vestimenti.

Finally, Ricketts and Wilder, with the knowledge gained of the approximate size of an organism which would not pass through the type of Berkefeld filter used by them searched the blood of human tabardillo patients for microörganisms, as well as the body contents of lice fed on such patients, and found an organism which is nonculturable with our present methods, but which has the shape of a short bacillus whose morphology is similar to that of the "hemorrhagic septicemic group." They say that while their results do not prove that the organism is the cause of typhus, yet the conditions under which they are found would justify further study.

In dark-field microscopic study of the fresh blood from our patients and in stained smears no organisms were found at any time. However, Ricketts was such a careful investigator that surely this part of the work should receive patient and careful investigation by all who are studying this disease.

Our own experiments, all of which were conducted in the laboratory of Mount Sinai Hospital, were made by Dr. R. Ottenberg, and deal only with monkey inoculations.

As previously reported, blood cultures in all our patients have

been negative, corresponding in this regard with the result of the experimenters just mentioned.

The monkeys used in our experiments were two Macacus rhesus, two Cebus capuchinus, and one Semnopithecus maurus. Inoculation of the blood of patients directly into the animals was done in two instances; 5 c.c. of blood drawn from the vein of a patient in the seventh day of his disease was injected intraperitoneally and subcutaneously into a Macacus rhesus, the monkey having been brought to the bedside and inoculation completed before the blood coagulated. This animal's temperature was taken daily for a month and showed no greater variations than those of another uninoculated healthy monkey. The animal was lively, and at no time appeared sick.

In the second experiment 5 c.c. of blood was drawn from another patient on the sixth day of his sickness. It was diluted with 10 c.c. of sodium citrate solution and injected intravenously into a semnopithecus. The temperature of this animal was taken at regular intervals for a period of three weeks; it did not show any pyrexia. These animals were kept under observation for two months during which time they were entirely free from illness.

Material obtained from the autopsy on the patient who had died on the tenth day of her illness was used for the other experiments. The animals injected with this material were one macacus and two Cebus capuchinus. The first received intravenously 5 c.c. of heart blood, the other two received intraperitoneally emulsions of liver and spleen, the one an emulsion of liver and the other an emulsion of spleen. The animals were kept under observation for three months, and showed no signs of illness.

While the results in all our experiments were negative, I would welcome other investigators carrying on a larger number of inoculations, with blood diluted with normal saline solution. Perhaps finally success may be thus attained and the disease prove to be inoculable. Until then we must consider our negative results of value in forming our judgment, and conclude that we are dealing with a disease in many respects different at least from the typhus fever of Mexico.

It does not seem necessary to compare this disease with tsutsugamushi, or the river fever or flood fever of Japan. The latter clinically bears certain resemblances to Rocky Mountain spotted fever (spotted or tick fever of Montana), but is distinct. The localized ulcer following the bite of the tick, a bright orange or a red mite called by the Japanese akamushi, a larval form of Trombidium, the involvement of the lymph nodes and the distinctive eruption would be sufficient to differentiate this disease.

Rocky Mountain spotted fever (spotted or tick fever of Montana) is also due to infection from the bite of a tick, Dermacenter occidentalis, and etiologically bears certain resemblances, yet impor-

tant differences to tsutsugamushi. "Both occur in small and usually strictly limited areas along certain streams running through mountainous country. The district in each instance is subject to heavy snowfalls in winter, and the streams to spring or summer floods. Along each infested stream the dangerous spots are usually more or less uncultivated, and the soil overgrown with underbrush, trees, or weeds, while the immune spots are well cultivated. Contagion is unknown in either disease."[5]

The Japanese fever always occurs after floods, being contracted on ground previously submerged by flood, whereas Montana fever either precedes or accompanies the floods. Infection in the former does not occur to those working on ground above the previously submerged ground; in the latter it is usually contracted on the hillsides high above the level of the river on unsubmerged grounds. The former is a disease appearing in July to October, the latter in March up to July.

The average mortality in both these diseases is very high, 30 per cent. in Japan flood fever and about 75 per cent. in tick fever of Montana.

I have always maintained that this type of acute infection of unknown origin more closely resembled typhus fever than any other disease known to me; that if it occurred during an epidemic of typhus fever, no differentiation could be made between it and that disease; that clinically the two diseases were very similar in onset, in duration, and in termination. The symptoms, which are alike, if not identical in both, are the headache, the period of fastigium, the continuous, steady, permanent pyrexia, and the critical fall, the eruption, the prostration, and the negative blood cultures. Nevertheless, the differences between the former and the latter furnish important differential factors which might indicate respective individualities. These are the periods of the year in which the former presents itself, being most prevalent in the months of the fall, and not in the late winter and spring, which mark the appearance of typhus fever. The appearance of typhus fever commonly occurs in epidemic or endemic form, which can be, indeed, denied of this disease. The factor of fatality in typhus which all observers place at a much higher figure than is our experience with this disease of unknown origin, which would predicate an almost negligible fatality—less than 1 per cent. in the latter against 15 per cent. to 60 per cent.[6] in the former. These are important factors of differentiation.

[5] Ashburn and Craig, A Comparative Study of Tsutsugamushi Disease and Spotted or Tick Fever of Montana, Philippine Jour. of Sc., B. Med. Sciences, January, 1908, iii, No. 1, p. 6.

[6] In this regard I would say that I showed Dr. S. Uhlfelder of Mexico City, some of my cases while he was on a visit to this city last summer, and he remarked that if he saw these cases in Mexico City he would say they were examples of tabardillo. On being told the very favorable prognosis of this unknown infection, he said that such a result was unknown in Mexico City, and that his own experience with Mexican typhus, which, I am told, is a large one, would justify him in placing its mortality at about 20 per cent. This alone would cause him to doubt their identity.

Again, the absence of marked nervous symptoms such as obtained in the epidemic form of typhus fever is a noteworthy distinction. Active delirium, paralysis of the sphincters, coma, or coma vigil, which mark the course of a pronounced typhus, have only exceptionally appeared in our cases. There are further epidemiological differences; these show that typhus fever is markedly communicable or contagious. It matters little whether we accept the recent idea that such transmission is through an intermediary host, such as the body louse, or not; it is a fact that the disease I described shows almost no evidence of communicability. This is important, because it occurs almost entirely among the very poor and pauper classes, where absolute personal cleanliness is rarely observed, and where one would suspect not only the presence of Pediculi vestimentorum to a greater or less degree, but a more intimate association of members of the same families necessitated by the confined spaces of tenement house abodes, which would be favorable to the dissemination of these parasites to more than one member of a family group, and thereby favoring at least the appearance of the disease in more than a single member of a family. The fact also obtrudes itself that, with the single exception noted in my previous contribution, no two cases of this disease have been observed by me in the same family or the same house. This seems to me strong evidence that the disease is not communicable either by contact or the bite of any insect. Finally, our experimental work in inoculating monkeys has at least so far established a fundamental difference between this group and Mexican typhus sufficient, perhaps, to stamp them as separate diseases. We still have before us the work to prove that the disease differs from typhus fever of the Old World. My attempts to obtain for this purpose an anthropoid ape have been unsuccessful, owing to their scarcity and the prohibitive price. I fear I shall have to leave the carrying out of the experiment of inoculating anthropoids to some endowed institutions devoted to research of infectious diseases. Should repeated inoculations into anthropoids with the blood of this disease fail to produce it, I think this evidence would be most convincing that the disease is one *sui generis*. While our own experiments were carefully conducted and their results may be relied on, the criticism may be made that they are not sufficiently numerous to justify any deductions. I shall await with interest the reports of other investigators, which I hope will be along the lines of animal inoculations. If their inoculation experiments confirm ours they will furnish added weight to the views here expressed as to the doubtful identity of this disease and typhus fever.

In conclusion, I would assert that, inasmuch as clinically the disease is similar to typhus fever, though the experimental evidence would appear to negative their identity, I still reserve in my mind the belief in the possibility of the development of an attenuated

modification of the virus of typhus fever. This attenuation in virulence could, I imagine, be induced by environment and improved sanitation to such a degree as to change to a great extent the clinical characters of typhus fever and the biological nature of its infectious agent. It may be that future investigators will prove this to be so, and thus be enabled to satisfy all doubts as to the true nature of the disease, which has been the occasion of so much interest to me, and securely place it finally in the at present undifferentiated group of typhus fever.

INTRAMUSCULAR AND INTRAVENOUS INJECTIONS OF ANTIMONY IN TYRPANOSOMIASIS.[1]

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The following experience is published now in order to place it within reach of those engaged in the study and treatment of trypanosomiasis. Later, a record of three and one-half years' observation upon this case of trypanosomiasis, in whom the above treatment was carried out, will be published in full.

Intramuscular Injection. The preparation used was metallic antimony in Lambkin's oily medium, received from Sir Patrick Manson, who procured it from Mr. Plimmer, who had tested it in the Lister Institute and used it in the treatment of syphilis in one of the British Military Hospitals. Ten minims, representing one-half a grain, of the precipitated metallic antimony was injected into the muscles of the left buttock. Within an hour the patient experienced great discomfort in the buttock, which increased until the whole buttock was greatly swollen, painful, and tender to such a degree that the least pressure of his body upon the bed, where he was compelled to remain, caused him to cry out with pain. Even with such cause removed the pain was so intense that morphine had to be used frequently. This condition, accompanied with sleeplessness, lasted for ten days, when the swelling, pain, and tenderness gradually subsided, and within fourteen days from the date of injection the patient was able to walk about, and two days later all inconvenience had disappeared. When the area of swelling had lost the tenderness sufficiently to allow of palpation, it was found to be tense, hard, and fairly sharply defined to a circular area of about 18 to 20 cm. in diameter. There was no necrosis. The temperature was as shown in the accompanying chart.

[1] Presented as a preliminary report before the meeting of the Association of American Physicians, 1911.

Sir Patrick Manson had recommended the use of the injection "once every one, two, three, or four weeks," the maximum dose being "20 minims of a 5 per cent. mixture, equal to 1 grain," beginning with "10 minims." From this experience, however, such treatment was impossible even had the patient not refused, which he did most emphatically.

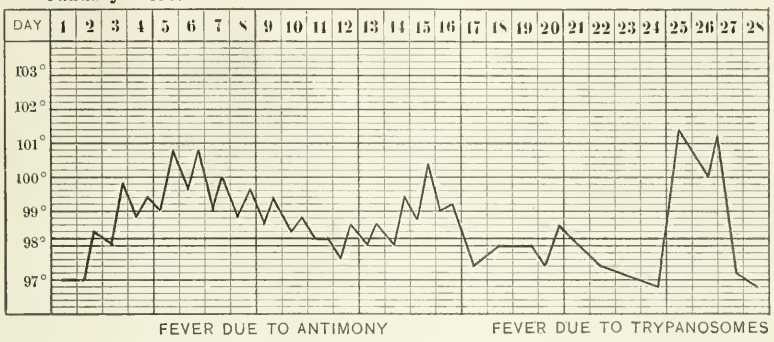

CHART 1.—January 3, 1909. Intramuscular injection (buttock) 10 minims = grain ½ of precipitated metallic antimony in Lambkin's oily medium; followed immediately by severe local pain and swelling, but no necrosis. Duration of symptoms two weeks.

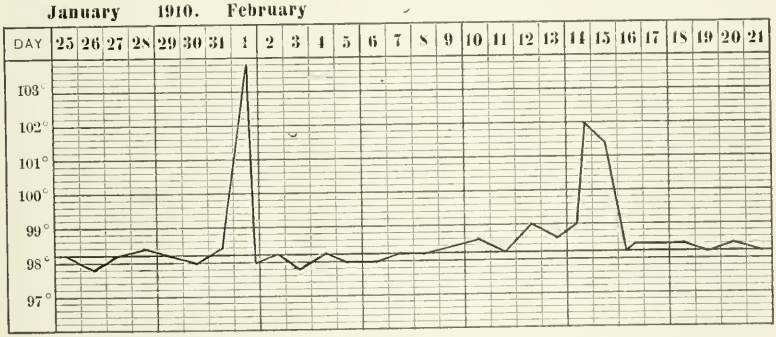

CHART 2.—February 1, 1910. Twenty minutes after an intravenous injection of ⅙ grain of antimony sodio tartrate (being the thirteenth injection since November 10, 1909) the patient was seized with violent nausea, abdominal pain, a chill, and great weakness. Temperature as above. Symptoms persisted five or six hours. On February 14 the same symptoms (less severe) occurred as on February 1. Trypanosomes absent. Indican in great excess. From October 9 to February 1, 1910, 1½ to 2 grains (in three pints of water) of antimony lithium tartrate were given by mouth daily.

Intravenous Injection. The preparation used was antimony sodio tartrate, also received from Sir Patrick Manson, who had procured it from Mr. Plimmer. One-sixth of a grain in normal saline solution was injected into a vein of the arm. From November 10, 1909, to February 1, 1910, thirteen injections were given, with intervals of about four days; on one occasion there was an interval of

sixteen days, on another an interval of eight days. The thirteenth injection was received at about 11 A.M., on February 1, 1910. About twenty minutes after leaving the laboratory, while on his way home, he was suddenly seized with nausea and great weakness. He managed to reach his home unaided. Before I could reach him he had had a chill and violent abdominal pain. When I saw him he was greatly prostrated, complained of intense headache, and had a temperature of 103.6° (see chart). This lasted five or six hours before subsiding to normal.

The blood was negative for trypanosomes. The urine showed a great excess of indican, otherwise it was normal. For twelve days the weakness and abdominal distress continued, and on the thirteenth day after the former paroxysm, he had for six hours a similar but somewhat less severe attack. Trypanosomes were not found at the time of this second febrile paroxysm, and have been absent upon all subsequent examinations. Blood and spinal fluid inoculations into monkeys, rats, and mice have been with negative results.

From October 9, 1909, to January 31, 1910, he took daily by the mouth $1\frac{1}{2}$ to 2 grains of antimony lithium tartrate in three pints of water, in addition to the intravenous injections.

Similar sudden but less severe and never alarming outbreaks of toxic symptoms occur (according to Todd[2]) with the administration of mercury. In the case here reported the manifestations were severe, alarming, and entirely without warning. The great excess of indican, had it been noted before the last injection, might have been a warning. The urine was carefully watched for signs of disturbed renal function, but with negative results.

The behavior of the disease subsequent to the antimony poisoning (?) was most important. From June, 1907, to November, 1909 (prior to the administration of the antimony), there were twenty-six febrile paroxysms associated invariably with trypanosomes in the peripheral blood. From that date the active antimony treatment, as recorded above, was begun, and except for the two rises of temperature occurring with the other symptoms of poisoning, no fever has occurred and trypanosomes have not been found in the peripheral blood or in animals inoculated with blood and spinal fluid. That is, parasites and fever have been absent for one and one-half years.

[2] Private communication, unpublished.

MACULOCEREBRAL DEGENERATION (FAMILIAL).

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A few peculiar cases have been reported which present a symptom complex sufficiently uniform and distinct to require independent classification. The one constant, characteristic manifestation is a degenerative process in the retinal macula frequently associated with a similar process in the brain. For descriptive purposes, the affection will be divided into (1) the maculocerebral type, in which both retina and brain are attacked, and (2) the macular type, in which the pathological changes are limited to the retina.

In the maculocerebral type the patient appears perfectly normal until the second dentition, that is, six or seven years of age, at which time simultaneous failure of vision and intellect ensues. Invariably, both eyes are affected. In developed cases the ophthalmoscopic picture consists of atrophy and pigmentation of the retina in the macular region, bleaching of the optic nerve, and narrowing of the retinal vessels. Small light spots, which do not present the appearance of exudates, may exist in the surrounding retina. Neither retinal hemorrhage nor edema has been described. The earliest ophthalmoscopic change is slight pigment disturbance in the retinal epithelium, which might be regarded as within normal limits. Even this change may be preceded by failure of visual acuity.[1] The functional eye disturbance consists of central scotoma for green and red, failure of central vision, and, sometimes, day blindness. As the disease advances the scotoma for colors increases in size, but does not extend to the periphery of the field. In the late stages the scotoma becomes absolute, and central perception of light is lost. Apparently the degenerative process does not extend to the anterior zone of the retina, and the peripheral field retains its normal boundary, vision, and color sense. As central vision disappears, the patient develops eccentric fixation, attended by nystagmus and lateral deviation of eyes and head. Both nystagmus and lateral deviation may diminish or disappear should the subject become completely imbecile and no longer endeavor to use the eyes. The failure of intellect varies from irritability to imbecility. In some cases epileptiform convulsions ensue. From the few cases reported, it would appear that the retinal atrophy commences in the macula and progresses rapidly for two or three years, after which it extends very slowly. In the brain the disease pursues a similar course, and after the intellect has sunk to the grade of medium imbecility its progress is retarded. No case has become completely blind, but some have become abject

[1] Stargardt.

imbeciles. So far as known, the cerebral degeneration does not cause death.

In the macular type of the disease the characteristic degeneration occurs in the macular region, but the intellect is not noticeably affected. It develops later than the maculocerebral type, usually during puberty, when the patient is from fourteen to sixteen years of age. One case, the earliest, commenced at the age of ten years. Reports also indicate that in the macular type the pupils are more active, and the nerve does not bleach so early as when the brain is involved. None of the patients was an epileptic.

In both types of the disease all the subjects have been reported otherwise in good health and free from malformations. In every instance the affection was confined to one or more members of a childship,[2] and not found among ancestors or descendants. Diseases which occur in this manner are termed "familial."[3] No case has been reported among Hebrews.

Maculocerebral Type. In 1907 I[4] presented the following cases before the Ophthalmological Section of the New York Academy of Medicine. The family history has since been corrected by more careful inquiry than was possible at that time. The childship consisted of three children, of whom the elder and younger were affected with maculocerebral degeneration, while the intermediate child, a girl, aged ten years, is intelligent and normal in all respects. The parents are not related by blood, but there is an indefinite history of intermarriages among ancestors. Father died from strangulated hernia and heart disease; was told by his doctor that he had Bright's disease; was subject to nervous seizures, attended by nausea and vomiting; vision good; father's brother is highly myopic; mother is in good health; never miscarried; she had an uncle born partly blind; no family history of syphilis, tuberculosis, or gout.

Case I.—February, 1907; girl, aged twelve years; brunette. She possessed good vision, and was an excellent scholar until the age of seven years, when vision and intellect began to fail. At the age of nine years she developed epileptiform seizures, which have continued at irregular intervals. During an intercurrent attack of mumps the convulsions were almost continuous.

Present Condition. Large, robust girl; no malformations; is a medium imbecile; talks well, and has a good memory for remote events; habits cleanly; myopic, −2 D.; pupils sluggish, but otherwise normal; has eccentric fixation, with head and eyes turned to right; lateral nystagmus; has neither night or day blindness, but cannot sleep in a lighted room. There is absolute central scotoma in both eyes, roughly estimated as 40° in right and 10° in left.

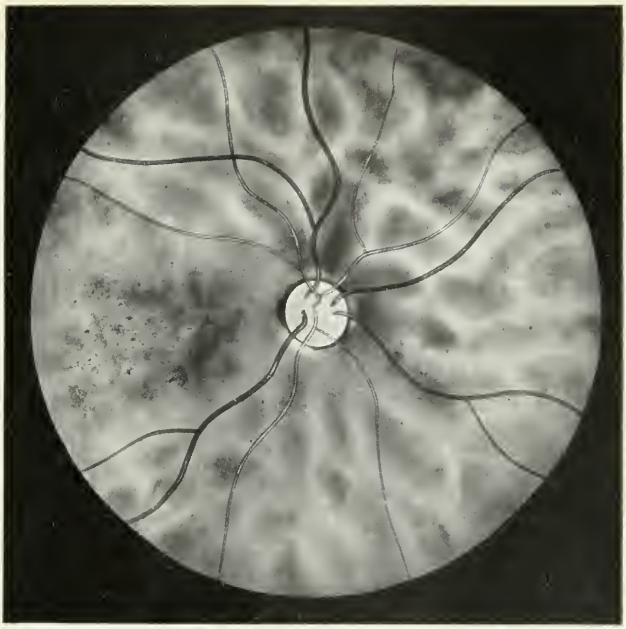
[2] Childship: All the children of the same father and mother.

[3] Familial disease: One that occurs among members of a childship but has shown little or no tendency to affect ancestors or descendants.

[4] Oatman, Arch. of Oph., 1907, xxxvi, 554.

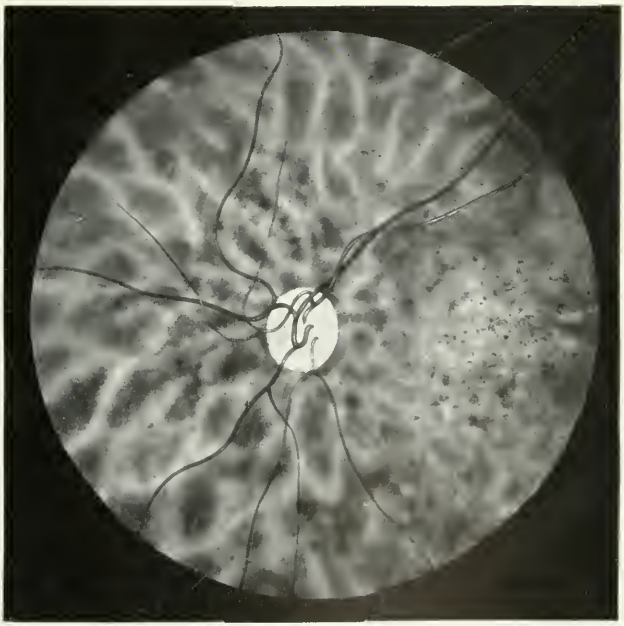
PLATE I

FIG. 1



Right eye of sister. Patient is a brunette, and the fundus, normally, is strongly tessellated. Of the four eyes described, macular degeneration is farthest advanced in this one.

FIG. 2



Left eye of sister. Macular degeneration and thinning of pigment slightly less than in right eye. The configuration of macular changes is symmetrical in both eyes, although differing from that seen in brother's eyes.

Peripheral fields are not contracted, and have good perception of white and colors.

Ophthalmoscope. Media clear; strongly marked brunette; tigered fundus. Optic nerve white and retinal vessels narrow. The macular region exhibits a pigmentary atrophy of the retina limited to an area with a diameter of about $2\frac{1}{2}$ P.D.[5] In this region the fundus is mottled with dirty, yellowish-gray spots and peppered with granular and dust-like pigment (Plate I, Fig. 1). Both eyes are affected symmetrically: in the right the retina is more atrophic, the fundus is lighter in color, and the pigment deposits are being dissipated (Plate I, Fig. 2).

May 10, 1910. Wassermann blood reaction for syphilis, negative. Von Pirquet for tuberculosis, negative. Intellect is very feeble. Vision appears worse, but examination unsatisfactory. Periphery of fields not contracted. Recognizes color of large red cloak. At the maculæ the retina is more atrophic, and the pigment deposits have mostly disappeared. The whole fundus is lighter, and by direct ophthalmoscopic examination light colored spots are seen on the retina, which appear and disappear on tilting the mirror.[6]

February, 1911. Wassermann reaction decidedly negative. Patient has almost reached the stage of complete imbecility. Memory poor for recent events. Saliva collects in pharynx and interferes with speech. Sings clearly and distinctly. Epileptiform seizures less frequent. Peripheral fields not contracted. Can distinguish red in large mass. Central blind area does not appear larger than in 1907. There is less nystagmus, and the eyes and head are held straighter. This apparent improvement is attributed to the fact that the patient is very apathetic, and has abandoned efforts to fix objects with her eyes. The retinal pigment as far as the equator is greatly thinned. The whole fundus is much paler than in 1907, and the choroidal interspaces are less pronounced. The central area is delicately veiled as though the retina had been converted into a fibrinous membrane. The retinal spots observed in 1910 have given place to unmistakable light reflexes. In the macular region the pigment has entirely disappeared, and several orange-colored choroidal vessels are exposed.

Case II.—February, 1907. Brother, aged eight years. Fair complexion. Was considered a normal child until six years of age, when failure was noticed in vision and intellect.

Present Condition. Excellent health; no paralysis; no malformations; hyperopic, +1 D.; vision: right, $\frac{10}{200}$; left, $\frac{8}{200}$; small cen-

[5] P. D.: Papilla diameter, or D. D., disk diameter. The optic disk is used as a standard of measurement in ophthalmoscopy.

[6] Both cases were examined at this time by the hospital neurologist, Dr. J. A. Booth. He found no disturbance of the nervous system except imbecility. Two years before this time Dr. Max Schlapp examined both children. His records state that they appeared to be somewhat ataxic.

tral scotoma for green and red; peripheral fields normal for white and colors; central fixation; talks well, and memory good.

Ophthalmoscope. Media clear. In the right eye (Plate II, Fig. 1) the macula is encircled by a transverse oblong ring of granular pigment, measuring about 1 P. D. in length. The enclosed area has a dirty, yellowish caste, and contains dark spots, which can be resolved into black granules. The surrounding retina is covered with dust-like pigment. The optic nerve is white, and retinal vessels narrowed. The left eye presents the same picture as the right, except that the macular retina within the pigmented ring is more atrophic and the fundus, as a whole, somewhat lighter in color (Plate II, Fig. 2).

May, 1910. Wassermann reaction for syphilis, negative. Von Pirquet for tuberculosis, negative. The degenerative process has greatly advanced in both retina and brain. Patient has become a decided imbecile. Has developed eccentric fixation, with nystagmus and eyes and head to the left. Central scotoma in each eye has become absolute. Peripheral fields good for white and colors. At the macula, the retina is highly atrophic and the pigmented specks have mostly disappeared, but small clumps of pigment are scattered through the surrounding retina. Nerve very white, and vessels attenuated.

February, 1911. Wassermann reaction negative. No paralysis. Deterioration of vision and intellect has slowly progressed. Memory poor for recent events, but remembers his first visit of four years ago. Is apathetic, and makes little effort to see. Eccentric fixation, with eyes upward. Nystagmus continues, but head is turned to one side. Retina contains fewer specks of pigment than in 1910. Has had five epileptiform convulsions, the first of which occurred three years ago.

The intermediate child is now fourteen years of age. She is a normal, healthy girl, with perfect visual acuity.

Cases of the maculocerebral type of the disease were reported first by F. D. Battin, of London,[7] in 1903, as "Cerebral Degeneration, with Symmetrical Changes in the Macula in Two Members of a Family." The father and mother of the patients were healthy English people. Mother never miscarried. The childship consisted of seven children, of whom the second and fifth were affected.

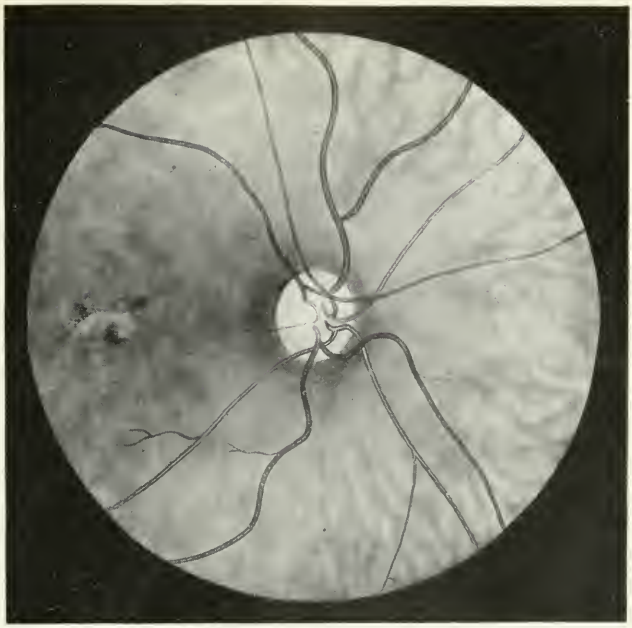
Case I.—Girl, aged seven years. Was normal until six years of age, when she developed a violent temper. No headache, vomiting, or convulsions.

Present Condition. Habits cleanly; speaks distinctly; is extremly irritable, and will shout for hours; no paralysis; central vision lost; peripheral vision and color sense are good. Pupils equal, with poor reaction to light. Occasional fine nystagmus. Eccentric fixation.

[7] Transactions Ophthalmological Society, 1903, xxiii, 386.

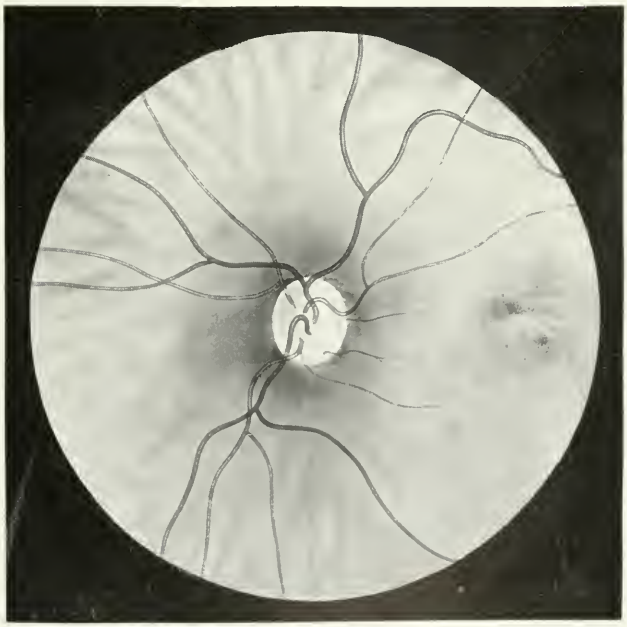
PLATE II

FIG. 1



Maculocerebral degeneration. Right eye of brother. This is the earliest stage of macular degeneration presented by any of the four eyes described in author's cases.

FIG. 2



Left eye of brother. Retinal atrophy is slightly more advanced than in right eye. The changes in the two eyes are remarkably symmetrical.

Ophthalmoscope. Examination by Lister. Changes similar in each eye. Media clear. Disks pale, but no evidence of previous neuritis. Peppered pigment all over fundus. At the macula is a reddish-black spot of about one-third the diameter of the disk. Its shape is irregular, and margin ill-defined. Retina around macula is pale and atrophic. Retinal vessels rather small.

Treacher Collins saw this case, and said the macular spot was due to actual pigmentation.

Case II.—Sister, aged ten years. Always in good health until six years of age, when she complained of headache. Three months later vision and intellect began to fail. About this time she had a convulsion, which has recurred twice.

Present Condition. Healthy child. Has slight nystagmus and lateral deviation of eyes (eccentric fixation). Pupils large and react slowly to light. Intellect defective, but talks well, and has a good memory.

Ophthalmoscope. Examination by Gunn: "The disks are pale and edges fairly distinct. Vessels are small, and there is some exudation along them. There is considerable pigmentation in the region of the yellow spot."

The subsequent history of these cases has kindly been supplied by Mr. Battin. Their vision and mental condition gradually deteriorated, and they were removed to the Darenth Asylum, where eventually they died. They did not become entirely blind. The cause of death was not ascertained, as Mr. Battin was unable to secure an autopsy from the asylum authorities.

M. S. Mayou[8] in 1904 reported three similar cases in a childship of seven children. Parents were first cousins. In her first pregnancy the mother miscarried at three months. The second, third, and fourth children were healthy, but developed maculocerebral degeneration, while the fifth, sixth, and seventh were both healthy and intelligent. The only evidence of syphilis lay in the mother's statement that at the time of miscarriage she had a sore throat.

Case I.—Boy, aged ten years. Was considered intelligent until six years of age, at which time he had measles. About this time failure of vision and intellect was observed.

Present Condition. The father states that the patient sees better at night. Counts fingers at two feet. Has eccentric fixation, and walks sideways. Occasional divergence of right eye. Pupils equal, dilated, and sluggish.

Ophthalmoscope. Media clear. Disks good color, but sharply defined. In each macula is a small reddish-black spot, surrounded by coarse black pigment. No changes at periphery. Eyes symmetrically affected.

[8] Transactions Ophthalmological Society, 1904, xxiv, 142.

Case II.—Sister, aged nine years. Was a normal child until six years of age, when deterioration of vision and intellect commenced.

Present Condition. Very dull, nervous child. Pupils equal and sluggish to light. Peripheral fields good for hand movements.

Ophthalmoscope. Changes symmetrical in both eyes. Disk pale. Same dark macula and granular pigmentation as in brother's eyes, although changes are more limited to centre of macula. Otherwise, patient is healthy.

Case III.—Sister, aged eight years. Very backward at school, but more intelligent than her affected brother and sister.

Present Condition. Pupils equal and sluggish. Alternating divergent strabismus. Central fixation. Hyperopic, +1.5 D. Vision in each eye, $\frac{6}{36}$. Fields for hand movements good.

Ophthalmoscope. Faint stippling at macula.

Six years later Mr. Mayou courteously writes as follows: "My cases are still alive, and the eye condition remains stationary. The eldest child has become a complete imbecile, and the other two children are in schools for the mentally defective. The mental condition appears to have a slowly progressive tendency, but the children are not blind."

Stephenson,[9] discussing Mayou's cases, stated that he had seen one instance of the affection in a girl, aged twelve years. There was parental consanguinity.[10]

Nettleship[11] describes the following case (No. 9 of series), which evidently belongs to the class under consideration.

Miss A., aged forty-eight years. Parents were first cousins. Patient is a twin, and one of thirteen children, of whom nine reached adult life. Of the nine, her twin sister and an elder brother have the same kind of bad sight as herself, and one of the others is an idiot.

Present Condition. Patient is feeble-minded. Has never seen well. Sees best in a dull light.

Ophthalmoscope. Changes in eyes, symmetrical. In the macula there is a large area of "epithelial removal," the outlines of which are irregular and ill-defined. No pigmentation or white spots in other parts of the fundus. Retinal vessels too small. Disk pale and waxy.

Nettleship remarks that "this case might well be claimed as an extremely atypical form of retinitis pigmentosa, with changes confined to the central region."

Hirschberg[12] reports the case of a boy, aged fifteen years. The parents were sisters' children. Not Hebrews. Mother never

[9] Transactions Ophthalmological Society, 1904, xxiv, 144.

[10] It was also stated that Still and D. Gunn had exhibited similar cases at a previous meeting, but they do not appear in the transactions of the Ophthalmological Society.

[11] On Some Cases Possibly Allied to Tay-Sachs' Infantile Retinitis, Transactions Ophthalmological Society, 1908, p. 76; Abstr. Arch. of Oph., March, 1908, p. 248.

[12] Centralb. f. p. Augenh., January, 1904, p. 12.

miscarried. Childship consists of five children, all of whom are sound except the patient. Vision bad since youth, especially in the evening.

Present Condition. Strong, robust lad. Low, knobby forehead, Darwinian ear nodule, facial asymmetry, and deep palate. He is an imbecile, but works about the house, and is cleanly. Counts fingers at 0.3 M.

Ophthalmoscope. Bluish-yellow ring about each yellow spot, complete in one eye but not entirely closed in the other. Remainder of eye ground lightly stippled, and covered with fine pigment. Nerves white and arteries very narrow.

This is the only case in which it would appear that the patient saw worse in a dim light, and even here it is not made clear that he had hemeralopia.

Macular Type. As stated, the macular type presents the history and every clinical feature of this disease, except failure of intellect. The period of development, however, is delayed until the age of puberty.

Two examples described by R. D. Battin,[13] in 1897, appear to be the first cases of either type reported. The affection occurred in two brothers. The father said he once had syphilis, but the sons were entirely free from the usual stigma of specific inheritance.

Case I.—Male, aged fourteen years. Recent failure of vision.

Present Condition. No failure of intellect. Hyperopic astigmatism. Central scotoma. No peripheral contraction of field.

Ophthalmoscope. Optic disk, pale. In the macula is a pear-shaped, dark red patch dotted over with fine pigment. Eyes symmetrically diseased.

Case II. Brother, aged twenty-one years. Vision commenced to fail when fourteen years of age.

Present Condition. Intellect appears normal. Myopic, — 1.5 D. Central scotoma. Peripheral field not contracted.

Ophthalmoscope. Fundus presents the same picture as in brother's eyes, but more advanced. Fine chorioretinal changes over whole macula, with central deposits of fine dotted pigment. Symmetrical changes in both eyes.

In 1903 Mr. Battin stated that in both the above cases failure of vision first proceeded rapidly, but later the condition became stationary.

Under the title of "Family Progressive Degeneration in the Macular Region of the Eye," K. Stargardt[14] has published the histories of two childships, which are typical examples of the macular type.

The first childship consisted of four children, all of whom were affected. There was no family history of eye disease, consanguinity

[13] Transactions Ophthalmological Society, 1897, xvii, 48.
[14] Archiv f. Ophthalmologie, 1909, lxxi, 543.

of parents, or syphilis. In every case the retinal changes were practically identical in both eyes. Aside from the eye affection, the patients were healthy, free from malformations, and of average intelligence.

Case I.—Daughter, aged twenty years. Progressive failure of vision began when fourteen years of age.

Present Condition. Hyperopic, +1D. Vision: Right, $\frac{4}{50}$; left, $\frac{8}{50}$. Central scotoma for white and colors in right eye and for green and red in left eye. Peripheral field normal for white and colors.

Ophthalmoscope. Nerve white on temporal side. Macula contains an area measuring about 1½ P. D., covered with grayish-yellow flecks and granular pigment. Light lines radiate from the macula which appear and disappear as mirror is tilted. Delicate gray spots along temporal vessels, visible only by direct ophthalmoscopic examination.

Case II.—Son, aged seventeen years. Noticeable failure of vision for last year and a half. Six months ago vision was: Right, $\frac{8}{35}$; left, $\frac{8}{25}$. Small central scotoma for green and red. The only ophthalmoscopic change was slight irregularity of pigment at the macula, which might be considered normal.

Present Condition. Hyperopic astigmatism. Vision: Right, $\frac{8}{50}$; left, $\frac{8}{35}$. Increased central scotoma for green and red. Peripheral fields normal for white and colors.

Ophthalmoscope. Optic nerve appears normal. In the macula there is a quadrangular-shaped, grayish-yellow patch, with delicately pigmented margin, covering an area of about 1½ P. D.

Case III.—Daughter, aged fifteen years.

Present Condition. Emmetropic. Vision: Right, $\frac{8}{15}$; left, $\frac{8}{10}$. Central scotoma for green and red. Peripheral fields normal for white and colors.

Ophthalmoscope. In the macula there is a sharply outlined, circular, gray line, enclosing an orange-colored area, with a diameter of ¼ P. D. Surrounding retina covered with yellowish spots and amorphous pigment. Yellowish flecks along temporal arteries. Optic nerve, normal.

Case IV.—Daughter, aged fifteen years. Vision: Both eyes, with + 2 D. $\frac{8}{15}$. Small central scotoma for green and red. Peripheral fields normal for white and colors.

Ophthalmoscope. Foveal reflex has disappeared. The macula contains several yellowish-gray spots.

Stargardt's second childship consisted of five children, three of whom developed macular degeneration. Neither parental consanguinity, syphilis, nor eye diseases could be discovered in the family history. Except the macular disease, every member of the childship was intelligent, healthy, and free from malformations. The first born, a son, aged twenty-two years, had normal eyes.

Case I.—Son, aged twenty years. Good vision until twelve years of age, since when it has steadily declined, but the loss has been slight during the last year.

Present Condition. Good pupillary reactions. Myopic, —2 D. Vision reduced to fingers at 2 M. Can see as well as another at night. Eccentric fixation. Absolute central scotoma for green and red. Peripheral field normal for white and colors.

Ophthalmoscope. In the macula there is an area about the size of the optic disk, covered with dirty yellow spots and fine, granular pigment. In the macular centre is a blue-gray area in which a choroidal vessel is exposed. Disk sharply defined and white on temporal side. Retinal vessels appear normal.

Case II.—Son, aged eighteen years. Vision has been failing for the last five years.

Present Condition. Myopic —2 D. Counts fingers at 4 M. Pupillary reactions prompt. Central scotoma for green and red. Peripheral fields normal for white and colors.

Ophthalmoscope. Temporal bleaching of disk. In the macula there is a dirty yellowish patch of about $1\frac{1}{2}$ P. D., covered with clumped and dust-like pigment, and containing an exposed choroidal vessel. The surrounding retina contains whitish flecks below level of retinal vessels. Vessels appear normal.

Case III.—Son, aged fifteen years. Twin. Poor vision was noticeable when ten years of age, but parents think deterioration commenced earlier. Loss of vision has progressed very slowly since the age of thirteen years.

Present Condition. Myopic, −1 D. Vision: Right, $\frac{3}{3\,5}$; left, $\frac{3}{5\,0}$. Central scotoma for green, red, and gray. Peripheral fields normal for white and colors.

Ophthalmoscope. In the macula is an ill-defined area of about $1\frac{1}{2}$ P. D., containing yellowish spots and scattered amorphous pigment. Foveal and macular reflexes have disappeared. Retinal vessels appear normal. Twin brother died soon after birth.

Case III.—This appears to have commenced at an earlier age than others of the macular type. Inasmuch as the patient was myopic, and the parents naturally solicitous, observations as to the period of development may have been inacurate.

Stargardt cites the following case from Leber's records:[15]

Girl, aged seven years. Only child of consanguineous parents. Progressive failure of vision for past nine months.

Present Condition. Counts fingers at 3 feet. No hemeralopia. Poor color sense for green and red. Periphery of fields not contracted.

Ophthalmoscope. Disk white on temporal side. Retinal vessels narrow. Macula shows fine alterations in retinal pigment, and small

[15] Unpublished case cited by Stargardt.

light flecks. Periphery of fundus normal. Both eyes symmetrically affected. Three months later she was much worse, and periphery of fundus showed rarefaction of retinal pigment. Leber considered the case an atypical retinitis pigmentosa.

Pathological Anatomy. In the absence of a microscopic examination the histological changes can be surmised only from the ophthalmoscopic picture. This indicates an atrophic degeneration of the retina, commencing in the outer layers. The earliest visible change is loss of the foveal reflex and rarefaction of pigment in the retinal epithelium. The loosened pigment is next distributed in the retina as a fine dust or specks which exhibit little tendency to wander inward over the retinal vessels. The pigment does not proliferate, neither is it fixed, inasmuch as it eventually disappears. Ultimately the retina is converted into a thin cicatricial membrane, and constitutes the delicate film which covers the macular region in advanced cases. When depigmentation is complete, the choroidal vessels are exposed. In my case, in which the choroid was thus revealed, the interspaces contained no pigment, although normally this was a strongly "tessellated" fundus. Depigmentation of the fundus oculi may be due either to local action of some adventitious substance, or the pigment granules may be removed by leukocytes.[16] The absence of all evidence of inflammatory action suggests that the retinal atrophy results from nutritive disturbance. Inasmuch as the retinal layer first affected is nourished entirely by the choroid, it might be inferred that the primary lesion is in the choriocapillaris. Furthermore, limitation of the pathological changes to the posterior pole of the eye corresponds to the distribution of a choroidal vascular circuit. Extreme interest attaches to the work of Stock (*vide infra*). In three cases of primary retinal degeneration he appears to have demonstrated by microscopic examinations that the primary change was a degeneration of the rods and cones, probably caused by selective action of some toxin in the blood.[17] No case reported indicates that the deep layers of the choroid were affected. The light spots described in many cases should be regarded as degenerative rather than exudative. They may have been due either to exposure and thickening of the lamina vitrea or to condensation and thickening of the retinal neuroglia. In Stargardt's and also in my cases the spots were not prominent and could be seen with the ophthalmoscope only by the direct method. Their tendency to fade as the light was moved indicated reflexes rather than actual deposits. Probably the optic atrophy is secondary to retinal degeneration, although, as regards cerebral cases, this is not certain. In my second case the nerve was white and vessels narrowed early in the disease. In the macular type, however, a late secondary atrophy is described. It

[16] I have seen complete depigmentation of the eyeground in a diabetic (Arch. of Oph., 191 . xxxix, 392).

[17] Possibly syphilis.

should also be mentioned that Wilbrand regards disturbance of the color sense and nyctalopia as evidence of disease in the inner layers of the retina.

Etiology. The records throw little light upon the cause of the affection. In one childship congenital syphilis was surmised, but not proved. Certainly, it did not exist in my cases. Racial predisposition, as in amaurotic family idiocy, may be excluded, as none of the cases occurred among Hebrews, but were distributed among various other races. Hereditary tendency to eye diseases did not prevail in any of the affected families. Blood relationship of parents may be measurably causative; thus, it existed in four of the six childships affected with the maculocerebral type, and in one of the four childships affected with the macular type. The fundus changes are not unlike those which occur in the aged, as though the retina were affected with a local, premature senility. Nettleship suggested that a cause for retinal degeneration in children might be found in nutritive disturbance due to the exanthemata or other exhausting conditions. In the pigmentary atrophies of the retina, Stock argues that an autocytotoxin exists in the blood, which exerts a selective action upon the rods and cones. Stargardt, applying this theory to his cases, suggests a toxin with a selective action for cones only. Dr. Max Schlapp, who observed my cases, also regarded the pathological changes as due to the action of an autotoxin upon the nervous elements of the brain and retina. It is important to note that the maculocerebral type appears with second dentition, while the macular type is delayed until the period of puberty. It is improbable that this is mere coincidence. More likely the developmental forces active during dentition and sexual evolution are here perverted to stimulate a latent degenerative tendency.

Differentiation. Several affections exist, which, while differing from each other, all bear some resemblance to maculocerebral degeneration. These are, hereditary macular anomaly, retinitis pigmentosa, amaurotic family idiocy, central chorioretinitis, and certain unclassified cases.

Hereditary Macular Anomaly. This condition has been well presented by F. Best,[18] who described the remarkable ophthalmological history of a family of whom 8 members presented a defect at the macula. In all other respects, however, the cases differed essentially from maculocerebral degeneration. The family was traced through five generations, and 59 individuals were examined, of whom, 31 presented some affection of the eyes.[19] The 8 affected

[18] An Hereditary Macular Affection, Zeits. f. Augenh., 1905, xiii, 199.

[19] Macular defects, 8; opaque nerve fibers, 1; one-sided amblyopia, 5; double amblyopia with nystagmus, 2; strabismus convergence, 3; pigment points in eye ground, 6; senile cataracts, 5; punctiform opacities at posterior pole, 6; ptosis and telangiectasis of lid, 1; glioma, 1; hypermetropia, 7; hypermetropic astigmatism, 8; anisometropia, 7. None of the cases was myopic.

with macular anomalies were distributed among 5 childships. The defect occurred by direct, indirect, and collateral inheritance.[20]

In 6 of the cases both eyes were affected, and in 2 the change was rudimentary and limited to one eye. In every case the defect was situated immediately below the point of fixation, a uniformity which Best regarded as a remarkable example of persistence in hereditary transmission. Among the cases with macular defect the following additional abnormalities were found: High hypermetropia, astigmatism, strabismus, persistent pupillary membrane, and one case of total color blindness. None of the cases had epilepsy, imbecility, or optic atrophy. Aside from the one case of total color blindness, the color sense was normal in all. Visual acuity was blunted, but none of the subjects was incapacitated. The poor vision had existed since early childhood, and was non-progressive. During eight years in which they were under observation no changes occurred in the eyes. From these facts Best justly decided that the condition was an hereditary macular anamoly.

Maculocerebral degeneration differs from such congenital defects in its family history, late development, progressive course, cerebral complications, central color scotoma, optic atrophy and invariable, bilateral occurrence.

Retinitis Pigmentosa. At first glance, maculocerebral degeneration appears like an atypical retinitis pigmentosa. Both affections develop in early life, are slowly progressive, and present a symmetrical picture of atrophy in each retina. Furthermore, it is estimated that 10 to 13 per cent. of retinitis pigmentosa cases are idiots. These analogies, however, are more than counterbalanced by the following features in which the two diseases differ. The most constant symptom in retinitis pigmentosa is night blindness. Supposititious cases, in which day blindness existed, are too few in number to vitiate the rule; the presence of this defect more than anything else has caused retinitis punctata albescens, retinitis pigmentosa sine pigmento, and gyrate atrophy to be classed as aberrant forms of retinitis pigmentosa. Opposed to this are 20 cases of maculocerebral degeneration, none of which had hemeralopia, while 3 saw better in a dim light. Retinitis pigmentosa is eminently hereditary, and the persistence with which it reappears in families renders it easy to trace its history. In maculocerebral degeneration, however, the family trees are remarkably exempt from eye diseases. True retinitis pigmentosa invariably commences near the periphery and all parts of the retina are invaded the macula last of all.[21] Macular degeneration, on the contrary, commences

[20] Direct inheritance: From parent to child. Indirect inheritance: From grandparents, uncles, or aunts. Collateral inheritance: Occurrence of the same anomaly among brothers and sisters; thus, familial disease occurs by collateral inheritance.

[21] Cases of Knapp (vide infra), Dujardin (Clin. Oph., 1904, p. 125), Scimmi (Annal. d'Ottal., xxviii, p. 69), and Sichel (Centralb. f. p. Augenh., April, 1897), reported as retinitis pigmentosa commencing at the macula, are lacking in other essential features of that disease and cannot be accepted as genuine.

in the macula, and does not appear to extend into the periphery. In retinitis pigmentosa the color sense fails only with light perception, but in maculocerebral degeneration one of the earliest manifestations is central scotoma for green and red. The idiocy associated with retinitis pigmentosa always is congenital, while the subjects of maculocerebral degeneration are born with normal intellects, which subsequently may be destroyed by the disease. Malformations of all kinds, common in retinitis pigmentosa, are lacking in maculocerebral degeneration.[22] Finally, retinitis pigmentosa is transmitted for generations, while maculocerebral degeneration is a familial disease.

Amaurotic Family Idiocy. Hirschberg remarked that his case presented some symptoms not unlike amaurotic idiocy, but differed in other and essential points. Nettleship, however, is disposed to trace a relationship between the two diseases. He suggests that amaurotic family idiocy may sometimes pursue a mild course and permit the child to grow up, and cited the cases of J. D. Battin and Mayou as possible examples. He avoided the racial difficulty on the supposition that Jewish blood flows in many gentiles. Apparently the two diseases are entirely distinct. Amaurotic idiocy appears to occur exclusively among Hebrews. Cases reported among other races have not been accepted as genuine. The lesion is a primary degeneration of the ganglion cells throughout the nervous system including those of the retina. The disease develops a few months after birth and eventuates in general muscular paresis, idiocy, and blindness, the patient usually dying within two or three years. In contradistinction to this history, maculocerebral degeneration develops in late childhood, and, so far, only among Gentiles. In no case has muscular weakness, paralysis, or ill health been attributed to the disease; neither has any case become entirely blind. Anatomically, the diseases differ essentially. Macular degeneration begins in the outer layers of the retina, and is limited to the central region. Amaurotic idiocy, on the contrary, begins in the inner layers and extends over the entire retina. By no means is it especially a macular disease; all regions of the retina are equally affected, but the opacity is most conspicuous about the fovea simply because here the dead ganglion cells are eight or nine layers in thickness as compared with a single layer elsewhere. The strong ophthalmoscopic picture thus produced appears to have engendered an erroneous idea that amaurotic family idiocy is a macular disease. Treacher Collins,[23] who saw F. D. Battin's cases, said the dark spot at the macula was composed of definite pigment granules, and was not due to contrast, as in amaurotic idiocy.

Central Chorioretinitis. The usual form of central choroiditis bears little resemblance to maculocerebral degeneration. Choroiditis

[22] Hirschberg's cases presented stigmata, not deformities.
[23] Transactions Ophthalmological Society, 1903, xxiii, 390.

frequently depends upon evident syphilis or tuberculosis. It presents inflammatory phenomena, and the early lesions appear as deeply situated foci of exudation. These are followed by formation of white cicatrices and massing of pigment. The history and course of maculocerebral degeneration have no counterpart in exudative choroiditis.

Unclassified Cases. Ophthalmic literature contains many unclassified cases, which may or may not belong to the same group as maculocerebral degeneration. The most important are the following by Stock.[24] Although regarded by the author as examples of an independent disease, it is strongly suspected that they were cases of congenital syphilis:

Four children in a childship were affected. No parental consanguinity. After the birth of the first healthy child the father acquired syphilis (statement very uncertain), and now is in America. The four patients were normal until they were six years of age, when vision and intellect commenced to fail. They exhibited posterior iritic adhesions and multiple glandular enlargements. The iritic adhesions disappeared after mercurial inunctions. No paralysis. One case was epileptic. They rapidly became absolute imbeciles, and completely blind. At first the fundus presented no visible change, but later pigmentation of the retina commenced at the periphery and extended toward the centre. One case became imbecile and blind within a year, without visible fundus changes, but slight peripheral pigmentation appeared later. The optic nerve and retinal arteries showed no positive evidence of atrophy. Three of the cases died from tuberculosis and the eyes were secured for examination, in one case an hour and a half after death. The findings were of the first importance in their bearing upon all forms of essential retinal atrophy. Optic nerves were normal. Choroid and inner layers of retina were comparatively free from degeneration. The only certain pathological change was more or less complete degeneration of the rods and cones. Degenerative changes in the retinal epithelium and emigration of pigment were regarded as secondary to destruction of the neuro-epithelial layer.[25]

This disease resembled maculocerebral degeneration in that it was aroused to activity during second dentition and manifested itself by the destruction of vision and intellect. It may be differentiated, however, by the presence of other eye lesions, constitutional taint, acute course, absence of optic atrophy, and primary location of the retinal disease at the periphery. The limitation of maculocerebral degeneration to the central zone is alone sufficient to separate the two conditions.

[24] Klin. med. f. Augenh., xlvi, 1, p. 225.

[25] Usually, it is uncertain that microscopic changes found in the rods and cones are due to disease. Postmortem degeneration and preparing the eye for examination generally causes more or less disintegration of these delicate structures.

The following case, reported in 1870 by Herman Knapp[26] as atypical retinitis pigmentosa, may have been familial macular degeneration, although the data are too incomplete for this to be assured.

Female, aged thirty-five years. Slow progressive loss of vision for last ten years. Parents not related.

Present Condition. Both eyes alike. No night blindness. Visual field not contracted. With eyes turned upward she can count fingers at 4 feet. Eccentric vision not impaired. Large central scotoma. Is red blind, but recognizes other colors.

Ophthalmoscope. A circular area in the macular region is whitish opaque and studded with bone-corpuscle-shaped pigment. Whitish and black specks are scattered over retina except in upper and outer quadrant.

In the ophthalmoscopic picture of maculocerebral degeneration neither the amount of pigment nor its arrangement has much bearing upon diagnosis. The essential point is the presence of "simple" as distinguished from postinflammatory atrophy of the retina, limited to the posterior pole.

Reports of ten childships exhibiting maculocerebral degeneration have been abstracted and presented. Considering that many of the authors wrote without knowledge of similar cases, the uniformity of their descriptions is remarkable, and justifies an attempt to segregate the disease from the multitude of unclassified cases in ophthalmic literature. That the two types described are modifications of one and the same disease is assumed upon clinical grounds. Possibly other cases separately described or altogether ignored should also have been included.[27]

Maculocerebral degeneration, undoubtedly, is very rare, but it is hoped that other cases will be forthcoming and our knowledge of the affection increased.

DYSTOCIA RESULTING FROM VENTROSUSPENSION OF THE UTERUS; FETAL DEATH; CESAREAN SECTION.

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The anatomical results of pregnancy in a uterus firmly fixed to the anterior abdominal wall are fairly uniform and may be stated as follows: (1) The only part of the uterine body which

[26] Transactions American Ophthalmological Society, 1870, i, 121.

[27] Vogt, Ueber familiare amarurotische Idiote, Monatsschr. f. Psych. u. Neurologie, 1905, Band xviii, p. 161; Band xxii, p. 495.

develops and expands to accommodate the growing fetus is that behind the point of suture to the abdominal wall; (2) the part of the uterine wall in front of and below the point of suture attachment is quite frequently found thickened and hypertrophied even to the extent in some cases of obstructing the parturient canal by the production of a muscular tumor; (3) The part of the uterine wall behind the attachment may become so thinned as to rupture during labor; and (4) the cervix is thrown upward and backward so that at full term it may be at the level of or above the sacral promontory. The suggestion of Noble that the farther back on the uterus the attachment is made, the greater its malformation and the more marked the dystocia, is true, in our opinion, though the converse is not, therefore, to be assumed as true, since the varying degree of the density of the fixation is an important modifying factor.

The forms of dystocia most commonly met with after fixation have been various fetal malpresentations; ineffectual labor, the cervix remaining undilated and high up, and, as has been noted above, there may be a thickened anterior uterine wall which alone may be an insuperable obstacle to delivery from below.

Mrs. R., aged forty-one years V-para. Previous labors easy; supposed to be about two weeks beyond term. She reported that she had had some irregular pains for several days past. There had been no show, and she had had a fair amount of sleep each night. Her previous labors have been normal. Examination of the abdomen showed a sharply marked forward projection of the pregnant uterus between the symphysis and navel, while the upper portion of the abdomen was somewhat scaphoid. A well-healed operative scar was seen in the anterior abdominal wall just above the symphysis. The woman gave the history of having had an operation some three years ago, and on inquiry it was reported from the hospital that the uterus had been stitched to the anterior abdominal wall, and that a cyst had been removed from the broad ligament. The abdominal examination further showed that the round ligaments ran upward and backward from the lower and most prominent portion of the tumor. No history was obtained of dragging during pregnancy on the scar. Vaginal examination showed that the anterior wall of the vagina was tense and somewhat bulging, and that the presenting part could be felt in the axis of the pelvis, while the posterior lip of the cervix could just be touched by the introduction of four fingers into the vagina, it being at the level of the promontory of the sacrum. It was obvious that delivery through the vagina was out of the question, as the cervix, pointing above the promontory, was firmly fixed, while the uterine axis was backward and upward. No heart sounds or movements could be elicited, and the patient stated that she had not felt motion for the last twenty-four hours. She was admitted

to my service at the Polyclinic Hospital, with the idea of performing Cesarean section the next day. Upon the afternoon of her admission, however, it was found that her pains had greatly increased in severity and frequency, the patient at this time stating that they were worse than those experienced in any previous labor. I therefore decided to operate at once. Had it been possible, I would have chosen some other method of delivery, as there was little doubt that the child was dead, and as there had been a number of vaginal examinations made previous to her entrance into the hospital, while the membranes had ruptured at some unknown period also previous to admission. As, however, the abdominal method of delivery was alone possible, special care was taken to cleanse the vagina after the patient was under the anesthetic, and it was packed with iodoform gauze, the latter being left *in situ* for twenty-four hours. Upon opening the abdomen the omentum was found adherent over the fundus and anterior face of the uterus below the fixation ligament. The latter was very dense, fascial in structure, about an inch in width, and perhaps one and a half inches in length. The fundus was held firmly in relation to the symphysis, and there was a marked posterior sacculation of the uterine body, which contained practically the whole child, with the exception of its head. The latter, after the severance of the fixation ligament, came into view in the lower uterine segment below a well-marked contraction ring. The walls of the uterus below the ring were dilated, and were closely applied to the head. The child was removed after delivery of the uterus, and was found to be slightly macerated and apparently somewhat beyond term, if its size and weight may be considered as criteria. Hysterectomy was performed because the uterus did not contract well after evacuation, because of the lack of tone in the sacculated portion. In a younger woman it might have been worth while to assume risks by leaving the uterus, which, in view of the patient's age, did not in this case seem justifiable. Her convalescence was entirely uneventful. The firmness of the fixation, as revealed by operation, justified the position which we assumed with regard to the method of delivery—namely, that nothing but the Cesarean section was to be considered, as the fixation of the uterus was so firm that any attempt to dilate the cervix would have resulted in uterine and bladder rupture.

The viciousness of the operation of ventrofixation during the childbearing period is well exemplified by this case. A multipara whose previous labors have always been normal is given by the operation an insuperable obstacle to delivery, together with the possibility of early uterine rupture from thinning of the posterior and lower uterine segment. If this were the only instance known in which labor has been complicated by uterine fixation, it would alone be sufficient to condemn this prodecure during fecundity.

Those desiring to learn more of the evils which may follow its performance may consult the paper of Andrews,[1] a perusal of which will no doubt satisfy the most insatiable appetite. That the operation in the case reported was a deliberate fixation seems proved by the absence of any signs of infection in the scar, by the history of afebrile convalescence reported, and by the firm, broad band of fascia which formed the fixation ligament. We are, therefore, of the opinion that the present case was one in which a deliberate ventrofixation was performed in a woman in the child-bearing period, an entirely unjustifiable operative procedure.

We desire also to mention another case in this connection which was delivered some months ago; this patient had been operated upon for a retrodisplacement of the uterus, which was thought to be the cause of sterility. She soon became pregnant and passed through her pregnancy without any untoward symptoms. At the time of her labor, however, it became evident that the operation which was intended to have been a suspension had in reality resulted in a fixation, as within a few hours after her pains began (she had rupture of the amniotic sac as the initial symptom of labor) it was seen that the uterus was sacculated, it being protuberant and a transverse furrow being appreciable as passing across the anterior surface. Within eight hours after the incidence of pains it was necessary to deliver with forceps, as a uterine rupture seemed imminent, and the pains, though incessant, were futile. Careful inquiry into the history of the former operation revealed that undoubtedly there had been a postoperative pelvic peritonitis (constipation, abdominal distention, and fever). The cervix in this case was not displaced to any marked degree. Delivery was easily accomplished by the use of the axis-traction forceps.

We have here then two cases in which the operation of ventrofixation has resulted more or less disastrously to the processes of childbearing. In the first case the operation was by intention, while in the second it resulted from imperfection in technique. We desire, however, emphatically to emphasize that in neither of these cases was the difficulty the result of the operation of ventrosuspension; the first case was a deliberate fixation in a woman capable of childbearing, and is indefensible; the second resulted in a fixation because of technical error. Both then must be considered and discussed as fixations, not as suspensions. It is undoubtedly true that other cases could be cited in which the same unpleasant result followed the supposed suspension, through some variety of infection; but in our experience, and from a study of the literature, we find that these untoward happenings have been so few as compared with the vast number of successful cases that they may be considered as a negligible factor. Certainly no

[1] Jour. Obstet. and Gynecol. of British Empire, 1905, vol. viii.

operative failure resulting from avoidable errors in technique can be advanced as an argument against the procedure itself.

It must be borne in mind that, as is true of all other surgical procedures, there is both a right and a wrong way to perform ventrosuspension. The sutures should be placed to include only peritoneum, and a very small amount of the rectus muscle on either side of the wound and the bite of uterine tissue must be in the apex of the organ midway between the tubal origins; moreover, the uterus must not be grasped by a tenaculum to facilitate suture introduction. These cautions may seem superfluous to one who has not followed the literature of this operation, but it is a remarkable fact that at the present day there are many who do not understand the differentiation between the suspension and fixation operations. In one of the recent numbers of a widely read foreign journal devoted to gynecology, an author of world-wide reputation, a strong partisan of the extra-abdominal shortening of the round ligaments, reports two cases to illustrate the ill results accruing from the performance of uterine suspension, although the slightest consideration of the case histories given will convince anyone that they were probably intended as fixations or at all events became such after operation. Again, a well-known author and teacher concludes in a recent article that suspension is unjustifiable during the childbearing period, and reports five cases to substantiate his attitude; and yet in these five cases in which Cesarean section was demanded, the so-called suspensions were performed by five different operators, and in only one instance is it known definitely whether a fixation or suspension was intended. Moreover, the same lack of discrimination has appeared in recent text-books, and it is, therefore, seen that in many quarters there is a want of perception with regard to this operation. The fact that in the earlier literature the term fixation was used to include all operations aiming to attach the fundus to the anterior abdominal wall may explain the rather remarkable lack of differentiation seen at times at the present day. There is no desire to veil the fact that accidents do happen as sequelæ of uterine suspensions, but the same may be urged against any other operation in surgery. It need hardly be again emphasized that any fixation operation upon the uterus during the child-bearing period is contraindicated, although in a recent volume even vaginal fixation is described without condemnation, and it must be admitted, that, although we have never personally encountered such a case, the suspension operation properly performed, and without subsequent signs of infection, may result in actual fixation, with all its evil consequences. Such are reported by operators whose reputation is beyond criticism; even the Kelly suspension, in which the peritoneum is alone depended upon, is indicated.

It is claimed by those who would entirely displace ventrosuspen-

sion that the area of adhesion between uterine fundus and abdominal wall may be broader than expected, and the resulting band be too firm to allow uterine mobility; that infection of the abdominal wound may fix the fundus and anterior uterine wall firmly to the abdominal wall, and finally, that a ventrosuspension which allows a normal delivery in the first subsequent pregnancy may later on become a fixation and produce dystocia so marked that Cesarean section may be demanded. Our experience, coupled with that of other operators, leads us to believe that the first and last objections just mentioned must be most exceptional, while we do not consider that the second is in any way pertinent, since it is certainly an evidence of poor technique if there be suppuration of the abdominal wound in such a case.

Finally, in support of our position regarding uterine suspension, we would refer to the paper by Polak, the most recent, and one of the best investigations of the subject within our knowledge. This paper was based upon 687 suspensions of the uterus. Among the number there were 416 women, in whom one, a part of one, or both ovaries with one or both patent tubes were retained; 52 pregnancies were recorded subsequent to these 416 suspensions, and the labor in 34 instances was attended by Polak himself. Among these 34 cases there was but one spontaneous abortion, one malpresentation, a breech; forceps were used but twice. In 31 of this number the vertex presented and the delivery was spontaneous in 29. In the 18 cases making up the remainder of the series of 52 pregnancies, and which were not attended by Polak himself, there were neither abortions nor malpresentations. With regard to the permanency of the operation, it suffices to quote the same author, who found but 8 per cent. among 301 private patients in whom a retrodisplacement recurred. Moreover, he was permitted to examine 47 of the 52 women subsequent to delivery, and in but 4 did he find the uterus retroverted. As the author remarks, and as will be agreed to by all obstetricians, this is a smaller percentage of backward displacements than is found after pregnancy in patients upon whom no operation has been performed.

We contend, therefore, that the small number of ill results in labor following ventrosuspension properly performed, as compared with the number of cases in which pregnancy and parturition have been normal, must be held as valid evidence in favor of the operation, and we believe that the ease and rapidity of its performance, together with the small incision required, and the transient period of anesthesia demanded, require its preservation as a legitimate surgical procedure.

THE USE OF ASCITIC FLUID FOR NUTRITIVE AND OTHER PURPOSES WITH THERAPEUTIC INDICATIONS.

PRELIMINARY COMMUNICATION.

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I. INTRODUCTION.

The results of some studies in hypodermic nutrition were detailed by the author two years ago.[1] It was shown at that time that nearly the entire protein requirement for a dog, with some added calories in carbohydrate and fat, could be furnished by means of fully peptonized milk, the dog at times being almost in nitrogenous equilibrium, and showing only a small loss in weight. It was found, however, that this method was dangerous, and its clinical usefulness was *nil*.

Since then two substances have been tried, by means of which it has been possible to supply considerable amounts of protein to the organism, apparently without danger, first by means of gelatin combined with varying percentages of amino-acids from meat proteose (the results of which are reserved for a future communication), the other by use of human serum in the form of ascitic fluid.

In these experiments the attempt has been made merely to supply hypodermically part of the protein demand, the caloric needs of the body being otherwise satisfied by additional amounts of fat and carbohydrates given by the mouth. As yet no forms of these latter substances have been found which would be readily absorbed and utilized, as it is well known that fats injected hypodermically are metabolized so slowly as to fail for immediate nutritive requirement, while the usual carbohydrates, such as glucose, dextrose, and lactose, are rapidly and almost completely excreted, only inconsiderable amounts being utilized.

The newer biochemical studies have shown that enzymes occur not only in the gastro-intestinal tract, but that they are contained in every tissue, and apparently also in every cell. That knowledge has given added stimulus to such studies as this, and although the complete solution of the problem of hypodermic nutrition is still out of reach, substantial advance has been made in the fact that we can supply a large part of the protein requirement. This

[1] Arch. Int. Med., 1908, i, 335.

is perhaps the most important step in tiding over conditions in which there is grave danger to life from great protein loss, combined with the inability to use protein when given by the mouth, as in acute gastro-enteritis in children, cholera, etc. Ordinarily in acute conditions the patients have enough reserve fat to furnish the necessary additional heat units, and, of course, this form of protein exhibition is primarily useful in acute conditions and for short periods.

The use of human serum either for therapeutic or nutritive purposes is not new, as a number of communications have been made from time to time on the former, either as blood serum alone, in small amounts, or the entire blood, as in transfusion. From a nutritional point of view much less has been done. Although Sutherland[2] speaks of serum in this connection, and remarks that there is evidence to show that it is metabolized, anything like exact data seem to be wanting. It is desirable, therefore, to make the nutritive value of human blood serum the subject of further investigation, and to discuss the indications for its clinical application.

The mere fact that any form of protein given subcutaneously cannot supply the full caloric needs is not an argument against such a use of serum, for if we can prevent the great protein tissue loss that occurs in certain conditions we shall have gone a long way in tiding over a period, in some illnesses when life hangs in the balance, and only a little help is needed to enable the patient to weather the storm.

It is also probable that this is not all, for blood serum, either normal or diluted, as in ascitic fluid, should greatly assist the organism in combating an infection, just as normal horse serum seems to help against some infections; and how much better, besides, to use an homologous serum than a foreign one, as there can be no danger from anaphylaxis or serum sickness, both concomitants, at times to the use of an heterologous product.

A chance demonstration of the nutritive value of ascitic fluid, or at least its usefulness in stimulating normal processes, was afforded the author in the course of some experiments on the effects of daily serum injections in a series of mice inoculated with mouse adenocarcinoma. The mice so treated gained in weight over the controls to a marked degree, and their general condition was so much better than the controls that the other laboratory workers had no difficulty in picking out the fatter, healthier looking mice from those which had not received the serum. So, too, in the use of the so-called Hodenpyl serum (a chyliform ascitic fluid from a case of carcinoma of liver and peritoneum) the patients injected for the attempted cure of their cancer almost invariably gained in weight and well-being for a time, quite aside from whether their cancer showed any par-

[2] A System of Diet and Dietetics, p. 297.

ticular change or not, demonstrating again that the nutritive value of serum, either as a food or a metabolic stimulant, is definite.

II. EXPERIMENTAL.

The Ascitic Fluid Used in the Author's Experiments. The ascitic fluid used in these experiments was obtained from cases of cirrhosis of the liver, free from toxemia of any kind. Transudates from cases of chronic endocarditis can also be used.

When used clinically, the cases from which the fluid is obtained must, of course, be free from syphilis, both by examination and the Wassermann test, and when there is any suspicion of tuberculosis, the fluid should be put through a guinea-pig. The tappings should be done with the greatest care to prevent contamination, as these fluids spoil very easily.

The nitrogen content should be determined, as this is found to vary within fairly wide limits, 0.17 per cent. to 1 per cent. of N. or more (blood serum contains about 1 per cent. N.), and first tappings are apt to be higher in N. content than subsequent ones from the same case.

The first experiment was on a dog weighing 6.5 kilos. The dog was put on the regular laboratory standard diet,[3] containing 0.6 gm. nitrogen per kilo of body weight and allowed to reach a constant weight before the injections of serum were begun. The urine and feces were collected by means of a metabolism cage. The data of this experiment are given divided into seven groups, corresponding to seven periods of different lengths.

The urinary nitrogen is taken as the index of nitrogenous metabolism. The feces from a normal dog contain comparatively little nitrogen, and from an animal on hypodermic feeding carry negligible amounts.

The feedings of protein were either by (1) mouth alone; (2) combined mouth and hypodermic injection; or (3) hypodermic feeding alone.

First Experiment.

Period 1. Three days. Regular diet.

Total nitrogen ingested	11.91 gm.	Total volume of urine, 710 c.c.
Urinary nitrogen	13.40 gm.	
Nitrogen balance	—1.79 gm.	
Loss in weight	0.70 gm.	

[3] Standard diet consists of lean meat in amounts of 15 grams per kilo (0.6 N. per kilo); cracker meal, 4 grams; lard, 3 grams; water, 35 c.c.; bone ash. This represents the usual full protein requirement necessary to keep a dog practically in nitrogenous equilibrium, with enough carbohydrate and fat to make up the caloric needs.

Period 2. Four days. Combined mouth and hypodermic feeding.

Total nitrogen ingested	15.88 gm.	Total volume of urine, 1134 c.c.
Total nitrogen injected	5.21 gm.	
	21.09 gm.	
Urinary nitrogen	19.80 gm.	
Nitrogen balance	+1.29 gm.	
Gain in weight	180.00 gm.	

Period 3. Three days. Regular diet.

Total nitrogen ingested	11.91 gm.	Total volume of urine, 991 c.c.
Urinary nitrogen	13.99 gm.	
Nitrogen balance	—2.08 gm.	
Loss in weight	210.00 gm.	

Period 4. Two days. Hypodermic feeding.

Total nitrogen injected	5.10 gm.	Total volume of urine, 192 c.c.
Urinary nitrogen	5.50 gm.	
Nitrogen balance	—0.40 gm.	
Gain in weight	310.00 gm.	(retained fluid)

Period 5. Three days. Hypodermic feeding.

Total nitrogen given	3.87 gm.	Total volume of urine, 765 c.c.
Urinary nitrogen	5.73 gm.	
Nitrogen balance	—1.86 gm.	(compare with Period 1)
Loss in weight	0.70 gm.	

Period 6. Three days. Hypodermic feeding.

Total nitrogen given	0.70 gm.	Total volume of urine, 1201 c.c.
Urinary nitrogen	5.05 gm.	
Nitrogen balance	—4.35 gm.	
Loss in weight	480.00 gm.	

Period 7. Two days. Nitrogen starvation.

Total nitrogen given	None	Total volume of urine, 548 c.c.
Urinary nitrogen	3.83 gm.	
Nitrogen balance	—3.83 gm.	
Loss in weight	220.00 gm.	

In this experiment a fluid containing 1.08 per cent. nitrogen was used, so it was possible to give a good quantity of protein without an undue amount of liquid.

The results of the different periods explain themselves, and it will be seen that the change from all mouth to all hypodermic feeding of nitrogen was not made at once, but the animal was

put on an intermediate period, combining mouth and hypodermic feeding.

The nearest approach to obtaining nitrogenous equilibrium was in Period 4, when the total loss was only 0.4 gm. for the two days. The variations in weight from day to day must not be taken too seriously, as the dog often held up a portion of the fluid injected, so unduly increasing his weight, and later secreted very large amounts of urine, accounting for a loss otherwise hard to explain. As a rule, the first few days showed a retention of liquid to some extent.

The nitrogen excreted from day to day varied only slightly whether the total quantity of urine was high or low. Although by mouth 0.6 gm. of nitrogen per kilo of body weight is hardly sufficient to keep the animal in nitrogenous equilibrium, judging from the results of Period 4, about 0.4 gm. of nitrogen per kilo in ascitic fluid would be sufficient by hypodermic. The difficulty, however, with such a procedure is that in giving large amounts of nitrogen by hypodermic, one has to inject a great excess of the fluid into the system, particularly if the percentage of nitrogen in the liquid is low. On this account, fluids of high nitrogen content are best, and it would be of advantage if some practical sterile way was found for concentrating the sera of low nitrogen to about that of normal blood serum. The fluid in this experiment was such (1.08 per cent. N.), that in Experiment 2 it was much lower, only 0.49 per cent. N., and the results were not so satisfactory:

SECOND EXPERIMENT.

Period 1. Two days. Regular diet. Weight of dog, 6.6 kilos.

Total nitrogen ingested	7.22 gm.	Total volume of urine, 404 c.c.
Urinary nitrogen	7.15 gm.	
Nitrogen balance	+0.07 gm.	
Loss in weight	0.00	

Period 2. Four days. Hypodermic feeding (nitrogen, 0.2 gm. per kilo).

Total nitrogen injected	5.32 gm.	Total volume of urine, 793 c.c.
Urinary nitrogen	12.55 gm.	
Nitrogen balance	—7.23 gm.	
Gain in weight	510.00 gm.	

Period 3. Two days. Hypodermic feeding (nitrogen, 0.1 gm. per kilo).

Total nitrogen injected	1.34 gm.	Total volume of urine, 965 c.c.
Urinary nitrogen	4.82 gm.	
Nitrogen balance	—3.48 gm.	
Loss in weight	470.00 gm.	

Period 4. Two days. Nitrogen starvation.

Total nitrogen injected	0.00
Urinary nitrogen	4.54 gm.
Nitrogen balance	—4.54 gm.
Loss in weight	250.00 gm.

Period 5. Two days. Regular diet.

Total nitrogen ingested	7.22 gm
Urinary nitrogen	7.08 gm.
Nitrogen balance	—0.14 gm.
Loss in weight	0.00

In the second experiment no attempt was made to furnish the full nitrogen requirement of 0.4 gram of nitrogen per kilo, only 0.2 gram per kilo being given at most.

The nitrogen excretion varied more in this experiment than in the first, and the result was not so satisfactory from a nutritional point of view as when the fluid of high nitrogen content was used. It is again seen, however, that nitrogen given in this way is absorbed—metabolized and excreted—and, therefore, is capable of supplying the nitrogen requirement of the system to a certain and often large extent. In both experiments the dogs received the regular allowance of cracker meal, lard, and water, as required by the previously explained standard diet throughout the periods, regardless as to whether they were getting nitrogen by mouth, hypodermic, or both, or none.

On one day in the first experiment and on two days in the second experiment the urine contained a trace of albumin, probably from the fact that part of the serum albumin failed to be completely metabolized, and was so excreted, rather than from a renal irritation. In both instances it occurred after the dogs had been fed for nearly a week by hypodermic injections of the serum, and was not accompanied by any rise in temperature or evident general disturbance.

In both instances the dogs remained well throughout the experiment, and showed no evidences of serum sickness, except when on large amounts of serum they were occasionally a little less lively, when also a transient edema about the site of injection might occasionally be seen for a few hours; this was, however, an exception.

III. GENERAL CONCLUSIONS AND THERAPEUTIC INDICATIONS.

No definite rules can be laid down for the clinical use of ascitic fluid, but a few important points have been suggested by these experiments.

It is apparently not advisable to attempt to give the full protein requirement by hypodermic, particularly if the nitrogen content of the fluid is low, as it necessitates injecting excessive volumes of serum, and under such circumstances a considerable portion of the liquid may be retained in the tissues, as edema, and the urine temporarily decreased in amount, thus interfering, for a time, with the necessary elimination of toxins in an infection. While apparently the excessive volumes do not cause a true nephritis, it is, nevertheless, a serious matter to hamper the filtration power of the kidneys. This does not take place when moderate amounts are given for short periods.

It is quite essential to give a fair amount of extra water to the system during the use of the hypodermic method, either by the mouth, rectum, or hypodermically.

It is best to begin with a single moderate dose and gradually increase to two doses daily, twelve hours apart, the actual amount depending upon the nitrogen content of the fluid. Since even 0.12 gm. per kilo[4] is the minimum upon which nitrogenous equilibrium can be maintained in man, it would require too great a bulk of fluid to meet this demand, as already explained.

Judging from a limited clinical experience, probably one or two doses only may be required to bridge over a desperate period. Probably also the daily dosage should not exceed 10 c.c. to 15 c.c. per kilo, depending on the nitrogen content.

For any possible stimulating effect on growth (as in marasmus) the dose should be small, perhaps 2 to 10 c.c. per day.

THERAPEUTIC ASPECT OF THE SERUM INJECTION.

It is too early to state with exactness the degree of usefulness of this method of using serum, for not enough clinical material has been collected from which conclusions can be drawn. The theoretical indications for its use may be suggested as follows:

1. In any condition in which there is need of protein which the organism cannot make use of when given in the ordinary way as food, but probably only for a short time.

2. In conditions in which the tissues are, so to speak, dried out, the percentage of fluid in the organs being lowered, as in intractable vomiting, diarrhea (acute), gastro-enteritis, in children especially, cholera, etc. Ascitic fluid, while weaker than normal blood serum, much more nearly meets the physiological demands than physiological salt solution, although it cannot probably be given in as large amounts. It is often advisable to give salt solution in addition.

[4] Chittenden, Science of Nutrition.

3. When the organism is being overcome by an infection for which we have not at present a specific antitoxin. Its usefulness here would be presumably by supplying a certain added amount of the normal constituents of the blood, antibodies, etc. These possibilities would probably be shown to have rather narrow limits.

4. When for some reason the growth of the body is interfered with by unknown causes, as in marasmus. The effect on the construction of body tissue, or at least the stimulating effect of the serum on this process, as shown in the cancer cases, both human and mouse, would seem to be quite distinct and beneficial when given in small amounts.

5. In blood conditions, such as hemophilia, hemorrhage, melæna neonatorum, where the hypodermic use of normal human serum has already been shown to be valuable,[5] with the added advantage that ascitic fluid is easily obtained in large quantities.

In the following section of this paper are given the results of the clinical use of ascitic fluid. At present it seems most useful in acute gastro-enteritis in children who are starved ("dried-out"), and suffering as well from infection in the digestive tract, in which condition the fluid seems at times to meet all three requirements.

CLINICAL EXPERIENCES WITH ASCITIC FLUID.

In order to demonstrate any possible usefulness of ascitic fluid as a food when given by the hypodermic route, a series of 9 children (8 suffering from the most extreme grade of acute gastro-enteritis or enterocolitis, and one from bronchopneumonia and enteritis) were treated by this method. It was though best to use it only in cases that had been treated unsuccessfully by the usual methods, and which consequently were in the terminal stages of the disease, in order that the test should be the most severe, so too that any improvement might perhaps be fairly and justly attributed to the treatment under trial.

Unfortunately, the series of cases is too small from which to draw definite or broad conclusions, and the results must as yet be taken only as a possible indication of what may be accomplished with more experience, recognizing at the same time that this same broader experience may fail to show consistent results.

The treatment was begun too late in the season to gather more data at present, so that the results are presented merely for what they are worth.

As in all new methods of treatment one must be morally certain that no harm shall result, so here, although presumably at least 0.15 gram of nitrogen per kilo of body weight must be supplied

[5] Welch, Blood Serum in Melena, Bulletin of New York Lying-in Hospital, 1910.

to attain anything like a nitrogen equilibrium, and it had already been proved that several times this amount could be supplied to a normal dog, it was felt that it was safer, in dealing with a desperately sick child, that only a fraction of the necessary amount should be given, until it could be proved harmless under more rigid conditions.

The plan adopted was to give one injection and to watch the results, stopping at that point if definite improvement was shown. Where the improvement was not so marked, repeated doses were given daily in increasing amounts. The nitrogen contents of the fluids used varied from 0.34 to 0.4 per cent. nitrogen.

Of the 9 cases treated, 2 recovered absolutely, and 1 showed almost immediate improvement, which lasted for a week, at the end of which the child died (Case II), although the improvement had been continuous up to the day of death and the patient actually gaining in weight. No discoverable cause of death was found post mortem, although the autopsy was not done by an expert pathologist. In all 3 cases the action of the ascitic fluid was apparently perfectly definite, and showed itself within a few hours of the time of injection. Even allowing that only 2 cases were helped, a percentage of 22 per cent. possibly cured in the face of such desperate conditions as existed in all these cases makes it at least worth further investigation.

Two cases (I and II) were given only one injection each of 30 c.c. of serum, 0.34 per cent. nitrogen; one case (No. IV) was given repeated doses for eight days.

The question of whether this method of treatment will find its greatest usefulness in giving one or possibly four or five injections, or, in giving it over considerable periods, possibly for a week, can only be settled by further experience.

The apparent usefulness of both methods was exemplified in the 3 cases that recovered. The 7 cases that died all received several injections, but to no purpose, as they showed no improvement.

Also the question as to whether it does more good as a food or simply by supplying added normal constituents to the blood stream must be still *sub judice*.

In conclusion, the author wishes to acknowledge valuable suggestions received from Professor William J. Gies, in whose laboratory at the College of Physicians and Surgeons the experimental work was done; also Drs. J. Rosenbloom, A. E. Sumner, N. R. Norton, E. Brownell, and H. Whitney, for assistance in furthering the work and in supplying ascitic fluid from suitable cases; and to Dr. R. S. Haynes, for data relative to some of the clinical cases.

I am especially indebted to Dr. Philip Van Ingen for his interest and his willingness to give the serum a trial in his hospital work. Most of the case reports were furnished by Dr. Van Ingen.

CASE REPORTS.

CASE I.—W. G., aged five months, admitted July 5, 1910. Diagnosis: marasmus, bronchopneumonia, and subacute enteritis.

Previous History. Fed on milk and barley water.

Present History. Began suddenly, July 1, with vomiting and fever; stools loose, brown. On admission showed marked emaciation; eyes and fontanelle sunken; rales over chest; prostration; toxemia marked. Temperature, 102°. Was given hypodermoclysis of 200 c.c. saline solution; caffeine, gr. $\frac{1}{4}$ hypodermically.

July 6. Slightly better, hypodermoclysis repeated twice today. Temperature, 103°.

July 7. Steadily failing since yesterday P.M.; weaker and pulse imperceptible; respirations shallow; apparently moribund; stools brown, loose. Has taken practically no food. At 11 A.M., 30 c.c. of acitic fluid, given hypodermically, as in all the series (0.34 per cent. nitrogen; 1.02 gm. N). Within one and one-half hours the patient's condition had undergone a rapid change for the better. Pulse was stronger and respirations normal. Temperature, which had been normal at time of injection, rose to 102°. Slight consolidation of right apex first noted today.

July 8. Improvement continues; can take food, and is apparently out of immediate danger. Signs of consolidation gone. Stools better.

July 11. Gradually improved, and began to gain weight. Temperature irregular, 99° to 102° until today, when it is normal. Taken home. Stools normal.

CASE II.—I. B., aged eight weeks; admitted August 18, 1910, 4 P.M. Diagnosis: gastro-enteritis and marasmus.

Previous History. Fed on cow's milk, and had long-continued gastro-enteritis before admission.

Present History. Same appearance as Case I; cyanosed; rales over chest. Pulse imperceptible at wrist. Heart sounds feeble Temperature, 98°; pulse, 82; respirations, 32. Child seemed moribund; no improvement in first two hours, on stimulation, with caffeine, gr. $\frac{1}{8}$; brandy, ♏ x. At 6 P.M. 30 c.c. acitic fluid given hypodermically (0.34 per cent. nitrogen; 1.02 gm. N). 7 P.M., condition markedly improved; not only stronger pulse, but less cyanosis, and cry was stronger. Temperature three hours after injection rose to 102°; normal next day; rose again to 101° on third day, then to normal. Stools at first green, with mucus, then became normal. Child gained weight, and was doing apparently well.

August 28. While doing well, suddenly within a few hours showed signs of weakness and collapse. Died ten days after admission and injection. Autopsy showed nothing to account for death.

No rise of temperature, and no evidence of infection. No symptoms of serum sickness.

CASE III.—J. G., aged two months, admitted July 30, 1910. Diagnosis: acute enteritis.

Previous History. Nursed one week. Last two weeks has had condensed milk.

Present Illness. Two weeks constipation and loss of weight. Weight, 8 pounds; in very poor condition.

July 30. Did very poorly, had a slight diarrhea for the next ten days.

August 10. Given 10 c.c. serum.

August 11. Given 15 c.c. serum. Weight, 6 pounds, 15 ounces.

August 12. Given 20 c.c. serum.

August 13. Given 20 c.c. serum A.M. and 20 c.c. P.M.

August 14 and 15. Given 20 c.c. serum A.M. and 20 c.c. P.M. Failed steadily. Serum discontinued. Died August 18. Urine gave great trace of albumin.

CASE IV.—C. W., aged thirteen months; admitted August 4, 1910. Diagnosis: acute gastro-enteritis.

Previous History. Nursed entirely for three weeks, then put on store milk; since sick has had only barley water.

Present History. Two days ago began to vomit and have loose stools. Up to that time was never sick. On admission, very poorly nourished; weight, 12 pounds, 1 ounce. Circulation bad; cyanotic; eyes sunken; abdomen sunken; great prostration; intensely toxic. Temperature, 99°. Stools light green. First twenty-four hours took practically nothing per os except water.

August 5. Serum, 20 c.c. hypodermically.

August 6. Took little water during day. Temperature 96.6°. Serum, 20 c.c. Distinct general improvement.

August 7. Given Eiweiss milk and water; took only a little at a feeding; vomited much. Temperature, 96°. Serum, 20 c.c.

August 8. Took feedings a little better. Temperature, 96.4° to 97.4°. Weight, 11 pounds 13 ounces. No vomiting. Serum, 20 c.c. Improvement continues.

August 9. Stools better; no vomiting. Temperature, 97° to 98°. Salt solution given. Serum, 20 c.c.

August 10. Vomited once and very restless. Temperature, 96° to 97°. Serum, 25 c.c.

August 11. Food about 4 grams at a feeding; no vomiting. Temperature, 96° to 97.4°. Stools normal. Serum, 25 c.c.

August 12. Same; no vomiting. Temperature, 97.4° to 100.4°. Castor oil given. No stools for twenty-four hours. Serum, 25 c.c.

August 13, 14, 15, and 16. Temperature, 97° to 101.4°. Continued to improve slowly. No more serum given. Developed ulcers on both eyes, and was transferred to Manhattan Ear and Eye Hospital. Did well there, and was discharged in fairly good general

condition, with normal stools. Urine examined several times thoroughly. No casts; very faint trace of albumin.

Case V.—B. M., aged three months; admitted July 26, 1910. Diagnosis: acute enterocolitis.

Previous History. Never nursed. Fed with milk and water, equal parts.

Present Illness. For past two weeks three to four watery, green stools daily; no vomiting. Weight, 8 pounds, 10 ounces; emaciated; very poor condition.

July 26 to August 8 slowly but steadily failed. Temperature 97° to 100.5°. Stools, three to six a day; loose, green, with some mucus. Serum given August 8 and 9, 20 c.c. each time. No effect. Urine, slight trace of albumin. Died August 9.

Case VI.—P. C., aged two and one-half months; admitted August 13, 1910. Diagnosis: acute enteritis.

Previous History. Nursed one week. Fed on condensed milk and later "Granum."

Present History. For four weeks had diarrhea; ten to fifteen green watery stools a day. On admission weighed 6 pounds 2 ounces. Temperature, 96.6° to 100.5°. In very poor condition. Given brandy, ɱ v every four hours. Took feedings well (Eiweiss milk). Stools, three to four a day; yellow and loose to green and loose. Failed slowly.

August 19. Serum, 15 c.c. injected; moderate redness of skin over site of injection. Discontinued. Died August 21. Urine, faint trace of albumin.

Case VII.—E. K., aged nine months; admitted August 11, 1910. Diagnosis: acute gastro-enteritis.

Previous History. Nursed three months, then store milk and water given since sick; rice water. Had measles a few weeks ago.

Present Illness. Began two days ago with vomiting and green stools. When admitted, temperature, 102.5°; pulse, 130 to 160; weight, 14 pounds, 5 ounces. Bad general condition. Stools, three to six a day; loose, watery. Vomited practically everything (water only given). Atropine given hypodermically.

August 12. Convulsion. Temperature, 103.6°; pulse, 160. Very poor condition.

August 13. Serum, 30 c.c. given. Died seven hours later. Urine not examined.

Case VIII.—A. T., aged six months; admitted July 7, 1910. Diagnosis: acute enterocolitis.

Previous History. Nursed one month, then boiled milk.

Present Illness. Very severe gastro-enteritis, with bloody stools. Was discharged in excellent condition July 28. Weight, 11 pounds 5 ounces.

August 1. Readmitted, with a second infection. Emaciation and prostration marked. Temperature, 102° to 104°. Weight,

9 pounds 14 ounces. Stools, five to eight a day. No blood at first, later occasionally blood streaked. Failed steadily for four days to August 5. Temperature, 98° to 101°. Was given strychnine and irrigations.

August 5. Serum given, 20 c.c.
August 6. Serum given, 20 c.c.
August 7. Serum given, 25 c.c.
August 8. Serum given, 30 c.c.
August 9. Serum given, 30 c.c.
August 10. Serum given, 30 c.c.

August 10. Condition had steadily failed. Temperature rose gradually to 106.5° on August 11, and death followed. Urine contained slight trace of albumin; just before death considerable.

Case IX.—P. W., aged seven months; admitted July 25, 1910. Diagnosis: acute enterocolitis.

Previous History. Nursed one month, then milk and water, equal parts.

Present Illness. Diarrhea for six weeks, ten to twelve stools daily, last week with blood. Vomiting occasionally. Weight, 8 pounds 12 ounces. Temperature, subnormal. Stools, four to six a day, yellow to green. Stools got better on Eiweiss milk. Steadily failed. Given serum, 15 c.c. on August 15 A.M. and 10 c.c. P.M. Not repeated (serum gave out). Died August 20. Urine contained only faint trace of albumin.

THE LEUKOCYTES IN THE EARLY OR PRE-AGGLUTINATION DIAGNOSIS OF TYPHOID AND PARATYPHOID FEVERS.

WITH A CONSIDERATION OF THE PATHOGENESIS OF INFECTIOUS DISEASES.

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Those wishing to advance our knowledge of infectious diseases must continue to shift the plans of their inquiries farther ahead, toward and into the incubation period. With the cure of the individual and the protection of the community as guiding principles, the search for early and still earlier information becomes self-evident and obligatory. Antitoxins, or antisera, depend for their efficiency upon early diagnosis, and we agree with Lüdke[1] in holding that the essential of prophylaxis is the early recognition of the infectious disease. All this applies particularly to typhoid, or paratyphoid fever, for the following reasons: (1) They must be differentiated early from pyogenic affections in order to avoid improper

therapy; (2) in order to institute at once curative therapy in the form of antisera, which the future, we hope, will bring us; and (3) to begin early and, therefore, most efficient prophylaxis. The typhoid bacilli are present in the blood of the patient from the beginning of clinical symptoms. Conradi-Drigalski found them even in the feces several days before the onset of typhoid fever. After knowing what to do we must begin to study how to do it. The purpose of this article is to demonstrate the early diagnostic value of the leukocytic changes in typhoid infections, and to present the clinician's side in the pathogenesis of infectious diseases in general, with special emphasis upon that of typhoid fevers. For the sake of clearness, it will be preferable to consider the latter first. There is a striking discrepancy between our knowledge of the biological properties of typhoid bacilli and the epidemiology of these infections, which is probably due to the fact that these germs behave differently in the test-tube than in the human body. It takes more knowledge and critical power than I possess to consider this question *in toto*. I shall, therefore, study it seriatim:

1. We must realize our own attitude toward typhoid fever. Bacteriologists and text-book writers have moulded medical teaching, and with it the student's mind in regard to the general conception of infection. The young practitioner has been taught to see typical cases, more suitable for schematic instruction than for reflection on the part of the student. The introduction of triads of symptoms, or of pathognomonic signs, have obscured the horizon of medicine. The search for cardinal symptoms has degenerated into an enumeration of signs without any reference to the varying significance. As Grawitz puts it: The clinician must decide, not the anatomist nor the bacteriologist. Of course, I do not wish to minimize the merits of the teaching profession, or to expatiate lengthily upon the limitation of well-known means of diagnosis. It is, however, urgent to remember the great importance of atypical, mild, abortive, or short-duration typhoid fevers.[2] The gastric fevers of German writers, the typhus levis or levissimus of Griesinger,[3] are of typhoid or paratyphoid nature. Upon the invasion of the intestinal lymphadenoid tissue by typhoid or paratyphoid bacilli depends the classical form of the disease. Between this and the mucous fevers, or paratyphoid infection, or some forms of meat poisoning, there is only a difference of degree. We all know of scarlet fever without the customary rash, or of Klebs-Löffler angina minus the membrane, or of pneumococcic sore-throat without any lung symptoms. Nobody doubts the contagious nature of these affections, in spite of their heterodox clinical characters. Individualism then in medicine, not dogma.

2. The second important fact in all typhoid infections is this: The marked biological, morphological, botanical, and pathogenic relationship between the numerous members of a large group of

hemiparasites[4] known as the colon-typhoid group. In this family the colon bacillus stands at the foot and the bacillus of Eberth at the top of the scale. Whether the latter occupies its place by reason of evolutionary development or because of a certain symbiosis, respectively, commensalism,[5] is as yet undecided. It is a fact, nevertheless, and has been demonstrated by the epoch-making work of Meinhard Pfaundler[6] in the group or family agglutination. His law of graduated elective specificity has been confirmed by many observers, Continental and American. Farther on I shall be able to show that the leukocytic alterations show a parallel relationship among members of the colon-typhoid group. There are two other and parallel phenomena demonstrating their generic relation—namely, the incubation period, increasing directly in duration with the rise of the germ from saprophytism to parasitism. Clinically, the condition known as typhoid since the days of Louis, develops the more frequently the higher in this scale the infecting colon-typhoid bacillus stands. (See Table of this group.)

THE BACILLI OF THE TYPHOID-COLON GROUP ARRANGED IN ORDER OF THEIR DEGREE OF PARASITISM.

The bacillus of true or orthotyphoid fever (Eberth-Gaffky).

The bacillus of paratyphoid fever, type A and B (Achard-Bensaude).

The Bacillus enteritidis of Gärtner, identical with the germs of mouse typhoid.

The bacillus of meat poisoning, type Westenberg.

The Bacillus enteritidis of Flügge-Känsche, identical with the pathogenic bacteria of the hog-cholera group.

The Bacterium flavosepticum of Brion-Kayser.

The bacillus of enteritis, type Danysz-Isaatchenko.

The Bacillus psittacosis of Nocard.

The Bacillus fæcalis alkaligenes of Petruschky.

The paracolon group of bacilli.

The Bacillus coli communis (Escherich).

No subject can be productive of more good than the serious consideration of the phenomena taking place prior to the clinical evidences of an infection. To ascertain the conditions of the host and the synchronous biology of the offending germ or germs during the period of incubation is a very serious task. We may rightly inquire into the conditions that would result in neither invasion nor infection in one case, a simple, short intoxication without morphological tissue changes in a second, and in typical infection with intoxication in the third case. Individual receptivity is undoubtedly of decisive importance in the genesis of infectious diseases. Just how often germs may invade the human body without

infecting it is as yet an unanswered question. There is, however, no infection without intoxication.[7] A disease which Clifford Allbutt wisely refrains from defining cannot be accepted as existing until we have perceptible proofs of its actual presence. The clinical onset of an infection, therefore, begins with the perceptible onset of subjective or objective symptoms. Thus, in pneumonia we date the onset of the disease from the initial chill, and in typhoid fevers from the appearance of the fever. But it is the incubation of the latter into which we wish to inquire. This is considered a difficult problem by H. A. Hare,[8] H. Curschmann[9] and others. H. T. Ricketts[10] believes that over 62 per cent. of typhoid patients show an incubation of over twenty days. It is more than probable that the higher any germ stands in parasitism in its own family the longer the incubation period. It is also my belief, which I expect to substantiate later on, that, at least for the colon-typhoid group, there is deepening leukopenia in direct proportion to the distance from the colon bacillus to the place in the family tree occupied by the bacillus of a given infection. According to Epstein[11] and others, in taking blood cultures in suspected typhoid patients it is important to decide (1) whether or not the offending germ belongs to the colon-typhoid group, and (2) then to ascertain its true place therein.

The succession of morbid processes—that is, the chronology of events in typhoid fever—I conceive to be the following: Its incubation is analogous to the sensitizing period in an animal injected with an alien proteid capable of acting as an antigen. The onset of typhoid fever depends upon the autogenous, auto-anaphylactic dose or doses of toxin injected during incubation in continual, minutest doses, and may be slow, insidious, as in most cases of true Eberthian infection, or fulminating, sudden in paratyphoid bacillus infections, or infection with the bacillus of meat poisoning of Gärtner. The final or third phase of an infectious disease is that of the clinical or mainfest stage, which in my opinion corresponds to the protracted anaphylactic period in an experimental animal. The fulminating cases of scarlet fever and of cerebrospinal meningitis may be taken as identical with the fatal anaphylactic shock observed in guinea-pigs. This theory of infection explains the pathogenesis of early clinical and preclinical phenomena better than any other schema known to me. It leads up to a fourth summary view upon the pathogenesis of the clinical symptoms and anatomical lesions in typhoid fevers. To go into details here would be beyond the scope of this report. Suffice to give here a few general conclusions. The mechanism of the fever of typhoid infection so well studied by Wunderlich has never been openly attributed to either the germ or its host, but Trousseau[12] already has spoken of the parallelisms between the fever curve and the Peyerian lesions of the intestines. This type of fever I believe to be an attribute of the intestinal lymphadenoid tissues of the patient, and not of the typhoid germs.

The leukocytic changes depend upon the characteristic alterations of the same tissues, of the same leukopoietic system of the intestines, and not upon this germ or its most closely related congeners. The white blood cell changes I consider as an anaphylactic phenomena, although Andrews[13] denies this. The causes of the early, marked typhoid splenomegaly are only partly known. The bacillemia, of course, and the roseola are part of the biology of the bacillus producing a given infection. The bradycardia has not been accounted for satisfactorily by any observer so far as I am able to judge from the literature. The peculiar characteristic intestinal lesions of typhoid fevers are, according to Dunschmann,[14] due to the irritating action of the typho-endotoxins eliminated by these lymphoid cells. It is a well-known fact, emphasized by Edsall[15] and others, that typhoid fever plays its role largely in the lymphatic tissues. Upon this fact, I believe, is based the leukocytology of all infections caused by the typhoid members of the colon-typhoid group.

It will now be in order to give a short outline of our present-day knowledge concerning paratyphoid fever. Atypical typhoid fever was well known to Lebert, Niemeyer, Liebermeister,[16] and others. It is fair to assume that many of these cases were due to the paratyphoid bacilli A and B, which were found first by Achard and Bensaude in 1896, and well established clinically by Schottmüller in 1899–1900. Since then a large number of cases have been reported here and abroad. The group phenomenon of Pfaundler has been repeatedly confirmed by Stober, Fox,[17] Gwyn, and L. Smith[18] in this country; Kayser, Foerster, Brion, Kurth, Kutcher, etc., in Germany, and Widal-Nobecourt and Lemierre[19] in France. The paratyphoid bacillus type B is the most important one clinically.[20] It occurs often as an acute gastro-enteritis, or as an acute meat poisoning.[21] The frequency of paratyphoid fever is shown by the following table:

TABLE I.

	No. of typhoid.	Paratyphoid.
Fox	500	8
Lehnhartz[22]	85	4
Schottmüller and Kurth	180	12
W. H. Bucholz[23]	61	26
Hultgen	25	7
Average	851	57 = 6.6 per cent.

I do not believe that only 6.6 per cent. of 850 cases of typhoid fever were due to the paratyphoid infections. Most of the latter are not reported, and as such not noticed officially. A large number pass as indetermined fevers, as walking or threatened typhoid fever, or as peculiar gastro-enteritides.[24] It is possible that 25 per cent. or more of all typhoid diseases, both in children and adults, are of the paratyphoid variety. There is a wide field of

fruitful research work open before the well-trained scientific general practitioner.

The diagnosis of paratyphoid fever is, as a rule, not difficult. Given a febrile disease, with clinically distinct typhoid features, a prodrome, accompanied by the characteristic leukocyte picture of typhoid infections, and showing persistently absence of the Widal reaction, one is justified in diagnosticating paratyphoid fever, thereby basing his conclusions upon the three before-going requisites. A blood culture yields, to be sure, more conclusive evidence, but it is hardly suited to the exigencies of general practice. Blood counting, however, may be learned sufficiently well within a week. The interpretation of all blood pictures will lose its air of mystery as soon as we shall have accepted the unicellular genesis of all leukocytes. Stober[25] says that owing to our lack of knowledge no hard and fast line can be drawn between typhoid bacilli and allied germs. This is true not only from the clinical standpoint, but as well from that of bacteriologists or serologists. It would, therefore, be wrong to officially ignore paratyphoid fevers.[26] The average total morbidity from paratyphoid is in all probability much larger than that of true typhoid fever, although the statistical mortality from the latter by far exceeds that of the former. I fully agree with Roger-Demanche,[27] Kayser, and others in considering paratyphoid cholecystitis as frequent in private practice. Paratyphoid carriers may be productive of much alimentary tract morbidity. At the present day a large number of paratyphoid cases are diagnosticated as acute gastro-enteritis,[28] as meat poisoning, or as ptomain poisoning, etc.

The diagnosis of true typhoid fever in its early stage is often difficult in large cities, in which the disease occurs only sporadically. Owing to the fact that the cardinal symptoms—namely, the Widal reaction, the roseola, the splenomegaly—occur simultaneously by the middle of the second week, it is strikingly evident that except for the bacillemia, in the majority of cases, there are eight, nine, and ten days of expectancy for the family physician. This often becomes uncomfortable to both the patient and his medical adviser. Eleven out of twenty text-book writers consulted state that the Widal reaction occurs on an average by the eleventh day of the disease. The same applies to the eruption and the splenomegaly. The diagnostic value of the agglutination needs not to be minimized, but to be readjusted. For Gruber it was a reaction of immunity, for Widal one of infection.[29] In all probability they are both right. The late appearance of this reaction very materially limits its diagnostic value in the first ten to eleven days. The following chart illustrates graphically the comparative synchronous diagnostic value of the bacillemia and the Widal reaction. The first, together with the leukocytic picture, is of value for early diagnosis; and the second for diagnosis after the middle of the second week.

TABLE II.—Bacillemia and Widal Reaction Compared as to their Diagnostic Value at the End of the Week.

	Bacillemia.				Widal reaction.			
	First week.	Second week.	Third week.	Fourth week.	First week.	Second week.	Third week.	Fourth week.
E. P Joslin[30]	90%	53.0% (732 cases)	40–60%	26–38%	rare	75.0%	85.0%	97.5%
Coleman-Buxton[31]	89.0% (224 cases)	73.0% (484 cases)	60.0% (268 cases)	38.0% (103 cases)				
Various authors	..	..	..	..	40-45%	85.0%	97.0%	98.0%
Stuhlern[32]	95.0%	60.0%	16.0%	7.0%				
H. Kayser	94.0%	56.5%	43.0%	16.0%				
Park[33]	..	..	..	..	20.0%	60.0%	80.0%	95.0%
Average	92.0%	63.1%	42.6%	23.0%	25.0%	76.6%	87.3%	91.0%

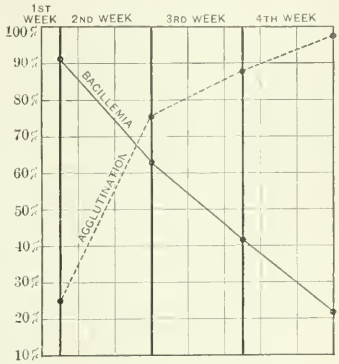

CHART I.—Percentage of positive blood cultures compared with the Widal reaction.

Statistics upon the agglutination reaction are probably not altogether reliable. A positive Widal test may be due to coagglutination of the bacilli of Eberth by allied germs such as the paratyphoid or Gärtner bacilli. Pfaundler gave all investigations upon the colon-typhoid group a new meaning and a new direction. In the near future, and with more material on hand than I have today, I shall further substantiate previous observations,[34] and demonstrate that the leukocytic changes in the true and paratyphoid fevers constitute another group reaction, and a parallel to Pfaundler's family agglutination, subject to the same laws. The conclusion is warranted that the higher in the scale of colon-typhoid parasitism a given causative germ stands the more will the leukocytic curves shift in the same direction. Courmont found that the first strains of typhoid bacilli are not agglutinated, which, according to Bail, may be explained by their aggressins. The disease itself is produced by interactions between the host and the infecting germs, and the Widal reaction considered by itself[35] is only one of the cardinal symptoms.[36] Even the bacillemia is, of itself, not sufficient for

identification.[37] F. Klemperer and A Brion[38] rightly insist upon the presence of that clinical condition known as typhoid since the days of Louis. Careful bedside observation is still the basis of typhoid-fever diagnosis, which, therefore, should be primarily clinical, then bacteriological. This applies to other infectious diseases as well—for instance, pneumonia, diphtheria, etc. When we shall have learned to trace back every symptom of typhoid fever to its first cause, the early recognition of these diseases will be an easier task. Once the genesis of incubation signs is discerned, we shall take less offence[39] at Delorme's attitude toward the evolutionary parasitism of the typhoid bacilli.[40] In advocating biliary antisepsis as possible and ideal prophylactic, F. Widal[41] unwittingly reiterated Murchison's pathogenic theory. Changes in our conception of the very genesis of infectious processes must of necessity be followed by some changes in our methods of diagnosticating them.

The Leukocytology of Typhoid and Paratyphoid Fevers. It is evident that biological and chemical tissue changes precede and foreshadow clinical symptoms. The leukocytes as the most sensitive and active derivatives of the mesoblast are, according to J. Renaud,[42] cytologically part of the general lymphatic system. They respond readily and invariably to every irritating alien proteid, according to conditions and laws as yet not understood. Alterations in the tissue juices and parenchymatous organs are promptly reflected upon the physiognomy of the blood. The regularity of their occurrence and the early appearance of the leukocytic changes in typhoid and paratyphoid fevers are striking. In fact, they are characteristic not of true typhoid only, but rather of the typhoid group of diseases. The study of the leukocytes as biological or biochemical indicators of these infections is, therefore, not merely useful, but essential in the early preagglutination diagnosis. From October, 1904, to September, 1910, I treated in my private practice 25 cases of typhoid fever, of which, 7 (or 28 per cent.) were due to paratyphoid infections. The latter gave at no time, during or after the course of the disease, a positive Widal reaction. Two occurred in children aged five and seven years respectively, two in adult men, and three in women. As many complete hemoanalyses were made as the patient and other conditions would allow. Pyogenic affections could thus be ruled out promptly and early. The reasons for this characteristic leukocytic picture of the typhoid group have been touched upon before.

The following numerical table represents the averages of all the leukocyte counts taken from 7 cases of typhoid fever and from 7 cases of paratyphoid infection. Appended to them, for comparison, are the figures from 50 white blood counts in 25 apparently normal individuals.

TABLE III.—Numerical Table Showing the Leukocytes in Typhoid and Paratyphoid Fevers and in Health.

	Typhoid.	Paratyphoid.	Normal.
Number of cases used in this chart	7	7	25
Number of counts	25	25	50
Total white blood corpuscles, average	5100	5000	7000
Polynuclears, average	62.0 per cent.	57.2 per cent.	64.2 per cent.
Small mononuclears, average . .	29.9 "	34.7 "	29.4 "
Large mononuclears, average . .	8.0 "	7.2 "	4.2 "
Eosinophiles, average	0.1 "	0.9 "	2.2 "

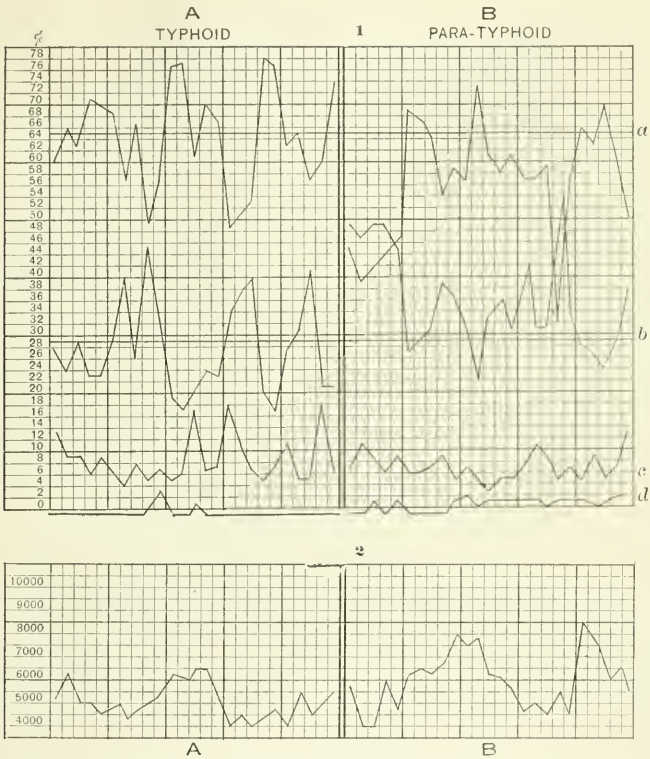

CHART II.—1. Comparative differential counts in typhoid and paratyphoid fever: *a*, normal polynuclear line; *b*, normal small mononuclear line; *c*, normal large mononuclear line; *d*, normal eosinophile level. 2. Comparative total leukocyte counts in the two diseases.

Chart II shows graphically the proportional leukocytic changes during the course of 7 cases each of typhoid and paratyphoid fever. Taken as a whole, we observe by these curves that the polynuclears are generally decreased and the mononuclears well increased at the time when the patient consults, or takes to his bed in a hospital. Uncomplicated typhoid infections have an initial polynucleosis, with a leukopenia, and within a few days a mononucleosis which persists until after convalescence. It illustrates also the constant leukopenia, the constant increase of large mononuclears, the absence

of eosoniphiles during the active stage of these two diseases, the ascendency of the mononuclears over the neutrophiles. The leukocyte picture obtained during any stage of typhoid fevers differs radically from that of pyogenic infections, hence its value in differential diagnosis. The fact that it approaches the type of leukocytic picture characteristic of early childhood speaks for the vigorous lymphadenoid tissue reactions in these affections.

CHART III.—Consecutive differential and total leukocyte counts of two cases of typhoid fever; the blood examined at short intervals during the entire course: *a*, normal polynuclear lines; *b*, normal small mononuclear line; *c*, normal large mononuclear line; *d*, normal eosinophile level.

Chart III is made up of the total leukocytic counts taken in two cases of typhoid fever throughout the entire course of the disease. It illustrates (1) in Case II the initial polynucleosis which Thayer and Nicolas-Balthazard[43] mentioned several years ago, and which J. Arneth,[44] according to his nucleo-analytic method, would call a hyperhypocytosis, that is, a leukopenia which a leukocyte picture shifted toward the right, that is, toward necrobiosis; (2) the early, marked, and persistent increase of the large mononuclears, which to many hematologists is a sign of bone-marrow reaction. To this theory of genesis for the large mononuclears, among which I always count the transitionals, I can in no way subscribe; (3) the total absence of eosinophiles during the first two-thirds of a typhoid

fever course is strikingly shown here. To this fact, O. Naegeli[45] called attention quite forcibly over two years ago.

The charts show at a glance the great similarity of the leukocytology of the two kindred infections. The following points may be set down as characteristic of the typhoid and paratyphoid group of diseases:

1. A leukopenia from the beginning, deepening gradually up to the fourth, fifth, and sixth week.

2. A moderate initial polynucleosis, lasting twenty-four to forty-eight hours, in uncomplicated cases, 67 to 78 per cent. of polynuclears being encountered.

3. Very early, but not initial, mononucleosis, progressive and marked, well into the fifth, sixth, and seventh week.

4. A well-marked, early, and persistent increase of the large mononuclears.

5. The eosinophiles are absent, early and persistently, until signs of recovery appear. They disappear abruptly with the onset of the fever, and reappear very slowly. Eosinophiles and bacillemia are evidently incompatible.

A priori reasoning would lead one to expect not only great similarity, but identity of the leukocyte curves in these two diseases; but the above higher polynuclear percentage and lower eosinophile curve of orthotyphoid infection may be due to three factors: (1) The blood counts were taken earlier because of the earlier morbidity; (2) the more frequently existing bronchitis, or other pulmonary complications; (3) co-existing mixed infections.

Conclusions. 1. It is probable that the incubation, conception, and course of an infectious disease take place according to the same laws that govern experimental anaphylaxis in animal.

2. The epidemiology of typhoid and paratyphoid fevers is still in its infancy. Statistics regarding these infections are unreliable and misleading, because their ingredient reports do not represent actual facts.

3. Our conception of the semeiology, the symptoms, and the anatomical lesions of typhoid fevers is faulty because the infecting germ is considered too much and its host neglected. A large number of typhoid symptoms do not depend upon the infecting germ, but upon the tissues electively affected by the intoxication or the detoxication incident to the disease.

4. The problems of early diagnosis in these fevers, and of efficient prophylaxis, is one for the intelligent, well-prepared general practitioner. Public hygiene is not exclusively a question of expert knowledge.

5. Any article or report upon the subject of typhoid fever without considering or appreciating paratyphoid infections must be judged as defective in scope and purpose.

6. Pfaundler's work upon the family agglutination of groups of germs has proved to be of inestimable help in the study of the real nature of infectious processes. The above leukocytic picture of typhoid and paratyphoid fever constitutes the cytological equivalent of Pfaundler's coagglutination and a parallel thereto.

7. The most important facts in the diagnosis of typhoid and paratyphoid fever are (*a*) the clinical condition known as typhoid; (*b*) the characteristic leukocytic picture; (*c*) the bacillemia, or blood culture; and (*d*) the Widal reaction. The importance of the four factors I consider to be in this order of sequence. It is evident that probably every case of typhoid can be diagnosticated a week or earlier before the Widal reaction appears.

8. The leukocytic picture of these diseases consist in the following: (*a*) Leukopenia, marked, early and progressive, very likely preceded for twelve to twenty-four hours by a slight leukocytosis. (*b*) Initial polynucleosis, lasting the first four to eight days, moderate in all uncomplicated cases. (*c*) A progressive and marked mononucleosis, displacing the polynucleosis, and lasting well into recovery. (*d*) A constantly present, well-marked increase in the large mononucleosis, which begins with the onset of the disease and disappears only after four to five weeks. (*e*) A sudden early and complete disappearance of eosinophiles in striking contrast to the leukopenia, is followed by very slow and hesitating reappearance synchronous with the first inklings of recovery. They disappear in relapses, and are of great prognostic value, both as to the severity of the disease and its duration.

9. The leukocyte picture of paratyphoid fever is almost identical with that of the Eberthian infection, being lighter in all its phases, parallel to the moderate intensity of all clinical paratyphoid symptoms. In both varieties this picture is so constant, and withal occurs so early in their course, that we may well call it the typhoid leukocyte picture.

10. Of 25 cases of typhoid fever in my practice, 7 (or 28 per cent.) were due to paratyphoid infection. This ratio, I believe, holds true for the typhoid fever situation of Chicago.

11. Careful, repeated double leukocyte counts afford the earliest reliable means of typhoid fever diagnosis for the general practitioner.

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REVIEWS

THE PRACTICE OF SURGERY. By JAMES GREGORY MUMFORD, M.D., Visiting Surgeon to the Massachusetts General Hospital; Instructor in Surgery in the Harvard Medical School. Pp. 1015, with 682 illustrations. Philadelphia and London: W. B. Saunders Company, 1910.

THIS text-book on the Practice of Surgery is designed for the use of those students only who already have learned by systematic instruction the theories or the principles on which successful practice is based. The author takes up the various departments of surgery in that sequence which brings to the front of the volume subjects which interest him most, or which he conceives to be of greater importance. The work is divided into seven parts: I. Abdomen. II. Female Organs of Generation. III. Genito-Urinary Organs. IV. Chest. V. Face and Neck. VI. Head and Spine. VII. Minor Surgery and Diseases of Structure. The entire field of surgery is covered, including such portions of gynecological and orthopedic practice as fall under the care of the general surgeon, but excluding the fields of higher specialization—eye, ear, nose, and throat. Dr. Mumford, however, clearly recognizes the limitations of the general surgeon even in orthopedic, neurological, and gynecological surgery, and is insistent in his teaching that only in cases of emergency, when no better advice is to be had, should a surgeon without special training undertake the management of difficult cases in these categories.

Each section is preceded by a short (occasionally not short enough) introduction, of historical and critical nature, in which the author's characteristics are shown to best advantage.

Careful perusal of the book shows it to be a safe, comprehensive, and modern presentation of the current teachings of surgical practice, founded on an experience evidently wide, tempered by ripe judgment, accurate reading, and a rare ability for epigrammatic expression. The following points have been selected for comment rather because they concern questions regarded still as *sub judice*, than because other topics are without interest.

The book begins with the subject of appendicitis, and to the amazement of many surgeons, indeed probably of most, the author advises gauze drainage in all early cases of appendectomy. "Do

not sew up the wound," he says. After forty-eight hours the wick is removed, and you may stitch the external oblique and skin if you choose, but if the McBurney incision has been used the tissues fall together of themselves. And this with an incision of "three of four inches." Incidentally attention should be directed to the false anatomical knowledge displayed in the illustrations of the McBurney incision, where the artist contrived not only to draw the internal oblique incorrectly in Fig. 8, but in Figs. 9 and 10 has succeeded in drawing it differently, but still wrongly. The "Ochsner treatment" is advised only in the case of apparently moribund patients: "In general terms every patient with diffuse peritonitis should be operated upon as soon as seen, unless in the judgment of an experienced surgeon, he is nearly moribund." When there is an abscess he opens it across the healthy peritoneal cavity, through a cofferdam of gauze. Both of them practices discountenanced by eminent surgeons, but which we believe to be for the best interest of the patient. If there is a hole in the cecum, Mumford establishes a false anus by sewing in a Mixter tube.

In the gynecological section, Mumford follows many general surgeons in regarding hysterectomy as the panacea. He urges this even in cases of acute metritis in puerperal or other forms of septicemia, and what is no less remarkable in cases of gonorrheal origin unrelieved by the curette. For extra-uterine pregnancy he urges operation before rupture or immediately after rupture; but says if there is profound shock the surgeon should "stand by" (a singularly well-chosen term, indicating that the surgeon is not to go home and dine out or go to bed, but to stay in the hospital and watch his patient) until reaction occurs, and then operate *at once.*

For cases of suspected syphilis he advises no treatment until secondary skin lesions make the diagnosis certain. While this, no doubt, is proper in *suspected* cases, we fail to see why the modern surgeon with laboratory facilities at command should not remove the suspicion by their aid, and at once begin treatment if indicated.

The section on the surgery of the lungs is scarcely up to date, but this is not surprising, as events have been moving with such rapidity in this department that practice can follow theory only as penalty, lame of foot, follows its victim, sure eventually to catch up.

Mumford commends in high terms the treatment of rodent ulcer by radium, assering that "of late we have come to believe that when exposed to radium the disease is aborted rapidly, and the *ulcer heals without leaving a scar.*" He recommends the injection of boiling water in the treatment of nevi, but if anybody held a syringe full of boiling water, as shown in Fig. 369, he would have his fingers boiled before the injection was begun. To say that "cut-throat" is "a bugbear of fiction" will give students a very false idea of what often is a mortal injury.

Writing of injuries of the head, he acknowledges *concussion* as an entity, yet says, "Should there be present unconsciousness or other evidences of cerebral disturbance, the surgeon had best turn back a flap of soft parts so as to determine the condition of the skull." Surely this statement should be qualified. At page 638 he has forgotten to insert the figure to which reference is made, showing Chiene's method of locating the Rolandic fissure.

The section on Minor Surgery is largely a reproduction, not to be regretted, of the author's popular Clinical Talks on Minor Surgery, published in 1903. There follow accounts of Diseases of Structure, including Vascular, Lymphatic, and Muscular Surgery, Tumors, Fractures, Dislocations, Bones, Joints, and Amputations. These sections are decidedly less good than the earlier portions of the work. They contain a needless amount of fine writing (and usually it really is fine, our only objection being that it is out of place), but the accounts of the various lesions are not always either exact or lucid. Yet the space occupied is well over two hundred pages—one-fifth of the book. But the author is essaying a difficult task in steering between systematic instruction, on the one hand, and operative surgery, on the other; and it is perhaps not surprising that sometimes he is carried into one current, sometimes into the other; that then, feeling he has gone too far, he sheers off as it were and leaves the discussion incomplete.

In the treatment of acute osteomyelitis it is questionable whether it is necessary or even advisable to curette and wash out thoroughly all involved marrow; many surgeons think the provision of drainage is sufficient, as in phlegmonous inflammation of soft parts. The statement that up to three years of age mechanical treatment is of little value in overcoming the leg deformities of rickets is not in accord with experience; rather should it be said that *after* three years of age the use of braces will accomplish little. In the treatment of pyarthrosis, aspiration and injection of formalin solution might well have been mentioned, even if the author does not commend it.

The volume is easy to read. Parts of it are fascinating. All of it holds the interest. Students who use it, provided they have already studied the principles of surgery, should be esteemed fortunate. Perhaps a little roughness in expression here and there will be corrected in another edition, *e. g.*, "The pathology of these conditions is similar often;" "Pelvic cellulitis leading to salpingitis even does occur sometimes;" "Divides the skin and sphincter ani even." There can be no doubt that a second edition will be demanded soon. The book will be widely studied, and with profit.

A. P. C. A.

DISEASE OF THE PANCREAS: ITS CAUSE AND NATURE. By EUGENE L. OPIE, Professor of Pathology, Washington University, St. Louis, Missouri; Formerly Member of the Rockefeller Institute for Medical Research, Pathologist to the Presbyterian Hospital of New York City. Second edition rewritten. 50 illustrations. Philadelphia and London: J. B. Lippincott Company, 1910.

DR. OPIE'S work, of which the second edition is now available, has certain defects as a text book. Chief of these is a lack of balance, a considerable amount of discussion being devoted to some sections, while others, equally important to the clinician, if not to the pathologist, are dismissed with brevity. The descriptions of the clinical manifestations of the various forms of pancreatitis are unsatisfactory. There is little system in the way the symptoms and signs are presented, and many signs and laboratory methods of considerable importance are either omitted entirely or are to be found only in other and somewhat unexpected parts of the book. As a series of monographs upon the various phases of the pancreatic question in which Dr. Opie has been particularly interested and toward the solution of which often he has been the most important contributor, the work must be commended highly. It contains an enormous amount of information gathered from literature and a detailed description of Dr. Opie's own discoveries, investigations, and conclusions that are most welcome to the investigator of pancreatitic conditions. A number of case histories are introduced that are remarkable for the scanty clinical data and the admirable pathological reports not an uncommon feature, unfortunately, of such histories. Two points that have chiefly interested Dr. Opie are the possibility of the causation of pancreatitis by a gallstone lodged in the ampulla and blocking the duct of Wirsung and the histological changes found in diabetes. He may well be pardoned his repeated reference to the former in view of his own early and important contributions.

In a book of this character it seems to me that certain subjects deserves either mention or more discussion. Thus the methods for detecting the pancreatic ferments in the stomach contents and in the feces are barely mentioned and are not described. The discussion of the Cammidge reaction, considering the very extravagant claims made for its diagnostic significance by some and the denial of either its usefulness or its specificity by others should have been given more consideration. Dr. Opie's attitude is apparently mildly favorable. The bulky fecal discharges should be noted under the symptomatology as well as under the section upon anatomy and physiology. More stress might have been laid upon the nonbacterial character of certain cases of acute pancreatitis, and the subject of therapeutics might have received some attention, par-

ticularly as a case is quoted in the chapter on physiology indicating the value of treatment with pancreatitic preparations. The excellent experimental work of Dr. Joseph Pratt apparently has confirmed these observations. Carnot who is an enthusiastic believer in the pancreatin treatment might also have been quoted upon this subject. An index of the authors whose writings have been used would have been an addition. The book is well printed. The illustrations are unusually clear, especially those of the histological section. It is indispensable to the student of the pancreas. J. S.

Diseases of the Nose, Throat, and Ear, Medical and Surgical. By William Lincoln Ballenger, M.D., Professor of Otology, Rhinology, and Laryngology, College of Physicians and Surgeons, Department of Medicine, University of Illinois, Chicago; Fellow of the American Laryngological Association; Fellow of the American Laryngological, Rhinological, and Otological Association; Fellow of the American Academy of Ophthalmology and Otolaryngology, etc. Third edition, revised and enlarged. Pp. 983; illustrated with 506 engravings and 22 plates. Philadelphia and New York: Lea & Febiger, 1911.

A medico-chirurgical text-book, the second edition of which has been exhausted within two years of the appearance of the first, as narrated in the preface to its third edition, has fully justified its emulatory competition with the great number of text-books which have preceded it on the same subjects. The present volume has been subjected to close revision of every page, and its illustrations have been enriched with sixty new drawings and five new plates, three being in colors. The colored plate illustrating translumination of the antrum is a complete success in conception and in execution, with all the definiteness of an absolute demonstration upon the actual patient. In fact nearly all the illustrations with which this work abounds are educational. The various steps of operative procedures minutely detailed are presented in sequence so that the student can learn the manipulations and observe their results as from the prosections of a masterhand.

In this way are taught the operations for resection of the nasal septum, for diseases and deformities of the accessory nasal sinuses and enveloping structures, operations of adenectomy, tonsillotomy, tonsillectomy, mastoidectomy, and some others.

Bronchoscopy and esophagoscopy are presented in brief but efficient detail, and therewith their utilization in diagnosis, in the removal of foreign bodies and in certain surgical procedures.

In almost all the subjects touched, the text has been brought

down to the very latest utterances, but alas! we failed to find any instruction on how to use the laryngoscopic and rhinoscopic mirrors or even the aural speculum, although there is at least one illustration of the speculum in use. It must be taken for granted that the reader is familiar with the manipulations of otoscopy, and indirect laryngoscopy and rhinoscopy, before he begins his studies in this volume.

The publishers are to be commended for the heartiness with which they have seconded, and the excellence with which they have presented the author's labors. J. S. C.

Modern Treatment. The Management of Disease with Medicinal and Non-medicinal Remedies. By Eminent American and English Authorities. Edited by Hobart Amory Hare, M.D., Professor of Therapeutics and Materia Medica, Jefferson Medical College, Philadelphia; Physician to the Jefferson Hospital. Assisted by H. R. M. Landis, M.D., Medical Director to the Phipps Institute for Tuberculosis and Physician to the White Haven Sanatorium. Volume II; pp. 900; 88 engravings, and 20 full-page plates. Philadelphia and New York: Lea & Febiger, 1911.

The review of Volume I of this work on therapeutics appeared in the last issue of this journal. The second volume is divided into ten parts, in the first section of which the treatment of infectious diseases, which was begun in Vol. I, is concluded by a discussion of those diseases that are due to parasitic agents, including syphilis and the dysenteries. Most of the remaining parts deal systematically with the treatment of the pathological states found in the various organs comprising the different systems of the body, as the circulatory system, digestive tract, nervous system, etc. There is, however, a fair-sized section devoted to a consideration of nutritional and metabolic diseases. The wise inclusion of chapters upon the non-surgical treatment of diseases of the organs of special sense, the skin, and the female pelvic organs well illustrates the comprehensive scope of the work.

As was the case in the first, so in this second volume, the contributors for the most part enjoy international reputations in their respective fields of activity. Therefore, although, as is but natural, one may here and there disagree with them in statements of minor details, upon the whole their opinions may truly be said to carry with them that authority which belongs to those whose researches and teachings have in many instances directed the trend of modern medical thought.

In the treatment of parasitic diseases, Craig had devoted fully half the section to a discussion of malaria, which is pardonable in one whose vast personal experience and painstaking labors in the study and treatment of this infection render him particularly well fitted to write about it. However, his enthusiasm for hemoglobinuric fever, which he regards as a disease *sui generis*, has perhaps led him to give an undue amount of space to this affection, whereas a disease of such economic importance as uncinariasis is dealt with in a scant three pages of text.

It will doubtless be a disappointment to some to find that Gottheil, in his article on syphilis, devotes scarcely a page to the discussion of the use of salvarsan, although he takes up in great detail the classic mercury and iodide treatment. It should be borne in mind, however, that when the present article was written, in October, 1910, Ehrlich's remedy was but a few months old and had only been employed in a small number of cases.

The selection of James Mackenzie to discuss the treatment of cardiovascular disease was a most happy one. No one has acquired a greater fund of accurate information, obtained by much precise personal observation upon all the varied phases of heart disease, than he. In this contribution he has cast aside the traditional empiricisms that have too long influenced our conceptions, or misconceptions, of cardiac disease and has dealt with the management of circulatory diseases from the standpoint of present day cardiac pathology. His consideration of drug therapy will be found refreshing. He is a warm advocate of large doses of digitalis, in cases suitable to its use, and he asserts, contrary to the common belief, that he has never seen this drug noticeably elevate blood pressure. A careful series of observations upon patients has convinced him that aconite is useless in the treatment of heart conditions. It must be confessed that his advocacy of 5 to 10 grains of chloral every two hours, as a sedative in certain cardiac cases, scarcely coincides with the generally accepted American belief in the depressant action of this drug upon the circulation. It is safe to say that the careful reading of Mackenzie's chapter would instil into many of us a helpful skepticism as to the efficiency of our present method of managing cardiovascular diseases.

In the generally adequate consideration of diseases of the blood by J. C. Da Costa more than passing mention might with advantage have been accorded the role of oral sepsis in the grave anemias and the importance of removing such foci of infection in their treatment.

The obtrusive feature of the section devoted to the treatment of nutritional and diathetic diseases is the careful scientific discussion of diabetes mellitus by Joslin. A noteworthy and surprising omission in this section is the entire absence of any reference to gout, a disease which would seem to be quite as deserving of

attention as either scurvy or obesity. In Volume I gout is briefly referred to in the chapters on dietetics and other general therapeutic measures, but nowhere is it accorded systematic consideration. It might not be amiss in another edition of this work to limit the discussion of the treatment of epilepsy, which is taken up by different authors in two separate places under nervous diseases, and devote the space thus gained to some suggestions as to the management of gout.

Coming as it does from one who has long been regarded both as a pioneer in the study of kidney diseases and a master in their management, the chapter on the treatment of nephritis, by James Tyson, is all that could be desired.

Much might be said of the various other portions of the book, which, although they have not been discussed specifically, are none the less deserving of such mention. It is to be hoped, however, that sufficient has been said to indicate that in the present volume, and its companion, the aim of both the editor and publishers to array the facts of modern therapeutics in such a way as to furnish the practising physician with a complete, reliable, and at the same time readily accessible guide to the treatment of disease, has been accomplished with entire success. G. M. P.

A Manual of Midwifery. By Henry Jellett, B.A., M.D., King's Professor of Midwifery in the School of Physic, Trinity College, Dublin; with the assistance in Special Subjects of W. R. Dawson, M.D., H. C. Drury, M.D., T. G. Moorhead, M.D., and R. J. Rowlette, M.D. Second edition; pp. 1210; 17 plates and 557 illustrations. New York: William Wood & Company, 1910.

This is a concise, practical exposition of the subject of obstetrics. The subject matter has been divided by the author into ten "parts," each consisting of several chapters. The first part, embracing over 100 pages, is devoted to a consideration of obstetric anatomy; the second, to obstetric asepsis, armamentarium, and diagnosis; the third, fourth, and fifth, to the physiology of pregnancy, labor, and the puerperium, respectively; while the sixth, seventh, and eighth cover the pathological aspects of the same periods. Part IX deals with the obstetrical operations, and the book closes with a section devoted to the infant.

While it is true that the work represents in general the teaching of the institution with which its author was formerly connected as assistant master, yet references to the work of others are found very frequently in its pages, and its list of "authors quoted" comprises

some 500 names. We do not find anything for adverse comment in the whole volume except in one instance, and this we believe was probably due to oversight; when speaking of the early symptoms of eclampsia, the statement is made that "it is advisable to examine the urine of every pregnant woman during the sixth and seventh month, and to ascertain the amount passed in twenty-four hours;" and, further, that "it is necessary to do so if . . . we have any grounds for supposing that she may be suffering from albuminuria." This just quoted paragraph is inadequate scientifically, and if followed will tend to create an indolent satisfaction in the mind of the practitioner, which will receive a rude awakening by the loss of a maternal life.

It seems somewhat unfortunate that, in common with several other recent authors, the use of a single series of interrupted sutures of silk is advocated as the method of closure of the uterine Cesarean wound. It has been amply shown by experience that this method will suffice in a long series of abdominal wounds, and yet there are but few operators of the present day who do not close the latter wound by the tier method of suture. The inference is certainly obvious. It would have enhanced the value of the otherwise very satisfactory chapter devoted to the infant had the infections of the newborn, particularly those associated with hemorrhage, been given adequate consideration. The author is to be congratulated that he has seen fit to advise against the senseless conservatism which sanctions the repeated use of the catheter after delivery, since the possible infection by far outweighs the remote chance of syncope after the second day.

While the book does not aim at exhaustive discussion of the subject, and therefore does not address itself especially to the relatively small class of men known as specialists in obstetrics, it is nevertheless amply sufficient for the needs of the great mass of the profession who deal with obstetrics as a part of their general medical work. It is one of the most satisfactory volumes published in the last few years. W. R. N.

Urgent Surgery. By Felix Lejars, Prof. Agrégé à la Faculté de Médecine de Paris. First English edition, translated from the sixth French edition. 20 full-page plates and 994 illustrations. Vol. II. New York: William Wood & Co., 1910.

Volume I of this work was reviewed in this Journal for July, 1910 (p. 117).

The present volume includes sections on the genito-urinary organs, the rectum and anus, the strangulated herniæ, and injuries to the extremities, with the more important luxations, fractures, traumatic hemorrhages, etc.

These subjects are treated in a manner which leaves, as a rule, little to be desired, if the teachings are considered as an exposition of present-day French methods and technique. Everywhere there is sound practical advice both as to conditions that are always "urgent"—such as traumatic hemorrhages—and as to conditions that are only occasionally so, such as prolapse of the rectum.

The apparent lack of familiarity of the author with the views and procedures of foreign—non-French—surgeons is as apparent in this volume as in the preceding one. For example, in dealing with luxations of the hip, no mention is made of Allis. The method of reduction recommended consists of: (1) "Progressive flexion of the thigh;" (2) "vertical traction on the flexed thigh;" and (3) "abduction and rotation outward." He says that usually this is the only plan that should be used, and describes it as "originally employed by Desprès père and afterward systematized by Bigelow."

It seems to us to combine portions of several methods, while failing to include the essentials of any. At any rate, he quite ignores the firm immobile fixation of the pelvis, which is undoubtedly one of the most important of the invaluable additions made by Allis in his study of this luxation. The author's idea of immobilizing the pelvis is shown in Figs. 245 to 248. A bearded assistant is, in three of them, leaning over the patient with his hands on the iliac spines. In the fourth, he has one hand on the front of the sound thigh. This alone would render valueless the whole procedure described in connection with these cuts.

The summaries of the symptoms of important conditions are often imperfect—*e. g.*, under subcoracoid dislocation of the shoulder no mention is made of Calloway's sign, the lessening of the axillary folds, or of Hamilton's sign, or of Duga's sign. It would be better to assume that the diagnosis has been made than to attempt to facilitate it and omit such important symptoms.

In describing catheterism for acute retention of urine, he fails to advise the distention of the urethra with oil—which makes so many "impassable" strictures pervious; the use of several filiform bougies when one alone fails to pass; and the employment of the tunnelled catheter. He nowhere sufficiently emphasizes the importance of the free administration of urinary antiseptics in conjunction with renal and urethra-vesical operations. While there is ample room for criticism of this character—as to omission of details, and particularly of those peculiar to the work of American and British surgeons—on the other hand, his explicit general rules are usually reliable, and, after all, he has described the technique that he and his confrères know and have employed. It must be admitted that if in a case of genuine urgency the practitioner must turn to a book for advice, it is better that he should not be confronted with opposing opinions or given a choice of methods. He will not be troubled in that way if he goes to this book, and he will usually get the help he

needs—whether the need arises from the fact that, as a surgeon, he lacks some particular experience, or, as a general practitioner, is unexpectedly confronted by a surgical emergency. J. W. W.

Recherches Experimentales sur les Tumeurs Malignes. Par le Docteur Jean Clunet, ancien interne de Hôpitaux de Paris. Paris: Steinheil, 1910.

The author describes in this book of 336 pages, experiments made with seventeen tumors of animals. The treatise is divided into two parts, the first part is purely experimental, dealing with the changes which take place in tumors during a series of inoculations, the result of excision of tumors upon metastasis formation, the visceral lesions in inoculated animals, and the immunity which an animal may possess against the tumor graft. The second part of the book is devoted almost entirely to a discussion of the modification brought about in tumors by the use of *x*-rays. The book is quite profusely illustrated with good cuts and contains much that would be of interest to one who is working in this field of research. W. T. L.

The Treatment of Syphilis with Salvarsan. By Sanitätsrat Dr. Wilhelm Wechselmann, of Berlin, with an introduction by Professor Dr. Paul Ehrlich, of Frankfurt-on-Main. Only authorized translation by Abr. L. Wolbarst, M.D., of New York. Pp. 175; 15 textual figures, and 16 colored illustrations. New York: Rebman Company, 1911.

This interesting book of Wechselmann's, the data for which is founded upon his personal experience in the treatment of some fourteen hundred cases of syphilis with salvarsan will be read with much interest by all, who for one reason or another, wish to obtain his views upon the subject. He, perhaps, is to be numbered among the most highly optimistic advocates of salvarsan treatment and his large experience is of great value in assisting one in judging of the merits of the drug. The entire subject is discussed in a most lucid manner. First there is a discussion of the results in the treatment of various types of syphilis with illustrative cases. Next the effect upon the Wassermann reaction is described. The complications of the intramuscular and subcutaneous methods of adminis-

tration are discussed and the contraindications summarized. The technique of the injection is detailed at length and in another section the elimination of arsenic discussed. Finally there is a review of the literature upon the subject and a summary of the results of other authors closes the book.

Until a few weeks before the publication of this book, Professor Wechselmann had used almost exclusively the intramuscular or subcutaneous method of injection, but since then, following the advice of Ehrlich, he has employed the intravenous method. He states that though this is much more agreeable for the patient, the effect upon the disease does not seem to differ from that obtained by the methods which he has used. Some of the results of treatment are graphically shown in 16 excellent colored plates. The book is well translated and printed. W. T. L.

Hématolyse et Hématogenèse, Bactériolyse et Bactériogenèse. Par Dr. S. Froin, ancien interne des Hôpitaux de Paris. Paris: Steinheil, 1910.

In this monograph of 250 pages the author sets forth a theory based upon cytological observations and experiments in hemolysis concerning the action of cells one upon another. He believes it is possible to show that with hemolysis of red blood cells by hemolytic sera, chemical substances are set free from the red cell which have a direct influence upon this variety of cell, influencing the red cells in such a way that their development and destruction is kept under control. The substances from the erythrocytes are specific and have no influence upon the leukocytes or lymphocytes which in turn possess their own regulating mechanism. The reasoning and conclusions are sometimes hard to follow, but the idea is quite new and very unexpected. W. T. L.

The Experimental Chemotherapy of Spirilloses (Syphilis, Relapsing Fever, Spirillosis of Fowls, Frambesia). By Paul Ehrlich and S. Hata, with contributions by H. J. Nichols, New York, J. Iversen, St. Petersburg, Bitter, Cairo, and Dreyer, Cairo. Translated by A. Newbold, and Revised by Robert W. Felkin, M.D., F.R.S.E., etc. Pp. 180; 34 tables in the text and 5 plates. New York: Rebman & Co.

This book of 180 pages purports to be an English edition of some collected papers by Ehrlich and his co-writers upon chemo-

therapy. There is a "Foreword" to the translation by Felkin in which one finds a rather objectionable use of "606" instead of salvarsan.

The volume opens with a chapter by Hata upon the experimental basis of the chemotherapy of spirilla with sections upon experiments with spirillosis of fowls and syphilis in rabbits. In the second chapter is a preliminary report by Nichols on "the action of '606' on Spirochæte Peternius in the animal body;" a section on "chemotherapy of relapsing fever," by Iversen, and a third section on the practical application of this method of treatment by Bitter and Dreyer. Finally the book ends with a summary of the whole subject by Ehrlich, to which is appended a bibliography that includes papers up to October, 1910. There can be no doubt as to the value of the contents of this comparatively small volume, but its method of presentation to the English public is far from what might be desired. The original German edition was published with as much expedition as possible, but the translation looks as if it might have been done over night. Indeed, the publishers seem even to have forgotten to date it. The translation is bad, sometimes almost ridiculous, and the text is very difficult to read. The book is poorly printed on cheap paper, and an objectionable catalogue of the publications by Rebman Company is found in the back. The "raison d'être" of the volume is too evident.

W. T. L.

Die Krankheiten der Nase und des Nasenrachens, mit besonderer Berichtsichtigung der rhinologischen Propädeutik. Diseases of the Nose and of the Rhinopharynx, with Especial Regard to Preliminary Rhinology. By Dr. Carl Zarniko, of Hamburg. Third edition; 8vo; pp. 744; 166 illustrations and 5 plates. Berlin: S. Karger, 1910.

This valuable text-book is divided into two main parts: (1) Propadeutic or preparatory essential, and (2) special pathology and therapy. The preparatory essential portion comprises first the subjects of the morphology, blood and lymph circulation, nerve distribution, and general histology of the nose and its accessory cavities, and of the rhinopharynx. This is followed by the general and special physiology of these structures and organs, and then the general pathology, symptomatology, diagnosis, and general therapeutics of their diseases are described and discussed.

The remaining two-thirds of the volume is devoted to its second part, Special Pathology and Therapeutics. The first section of the treatise and the pathological portions of the second section are extensively detailed, and so copiously annotated, with references

to the number of 2431, as to comprise an encyclopedic exposition of the subject matters. Yet this colossal grasp of material permits many important things to slip with bare mention or without mention at all, and occasionally includes a paragraph more amusing than practical. Thus, to go from grave to gay, divergence of opinion among practitioners as to importance of subject is nowhere shown in as great measure as in the text where Zarniko devotes twenty-eight pages to an elaborate consideration of the subject of adenoid vegetations, for removal of which the Gottstein curette is the only instrument advocated, and incidentally employs but two supplemental pages to discuss tonsillotomy, for which Physick's amygdalotome is the sole instrument described, while—will ye believe it without seeing for yourselves, ye American rhinolaryngologists and your disciples?—no mention whatever is made of tonsillectomy! Similarly, after discussing the propriety of turbinotomies in connection with hypertrophies, turbinectomy is denounced as a reprehensible mutilation. Yet Zarniko himself practises a submucous partial turbinectomy in cases of extreme hypertrophy, especially in conjunction with submucous resections of the nasal septum.

An amusing paragraph occurs where the author descants on the treatment for paroxysms of asthma; an American patent medicine being recommended with the announcement that a certain equally effective German imitation, of which the formulæ is given, can be purchased for one-fourth of the price of the original. The concluding phrase is, "So much for the treatment of the asthmatic paroxysm."

Nevertheless, this treatise is remarkable for the extreme care with which the anatomical constructions and relations and the pathological changes and conditions are discussed in their various aspects, so as to constitute an admirable and accurate guide to the student desiring to master his subject from the actual wet and dry specimens, and to the experienced practitioner simply desiring to freshen up.

Finally, the surgical technique and the operative procedures are described with such detail as to include all the contingencies likely to occur during operation and during after-treatment. Such instrumental diagnosis as the author practises is so fully described that the successive positions of patient, hands, and appliances can be appreciated. J. S. C.

Le Tronc Coeliaque, Recherche d'Anatomie Chirurgicale sur les Artères de l'Abdomen. Par Pierre Descampes, Prosecteur des Hôpitaux. Paris: Steinheil, 1910.

This complete description of the anatomy of the celiac axis is based upon a study of fifty subjects in which the arteries of

the abdomen have been injected. The usual course and the variations of each of the three main branches of the cœliac axis are discussed at first and later in separate chapters the ramifications and terminations of these main arteries are described. The book is profusely illustrated with black and white diagrammatic drawings. W. T. L.

The Optic Nerve and the Accessory Sinuses of the Nose. A Contribution to the Study of Canalicular Neuritis and Atrophy of the Optic Nerve of Nasal Origin. By Professor A. Onodi, of the University Budapest; Member of the Hungarian Academy of Sciences. Authorized Translation by J. Lückhoff, M.D. (Edin.), Ch.B., of Cape Town. Pp. 101; 50 illustrations. New York: William Wood & Co., 1910.

It is stated in the preface that this English edition of Onodi's valuable German monograph of 1906 increases the illustrations from twenty-seven to fifty, and combines the papers presented by Onodi to the First International Congress at Vienna, 1908, and at the Annual Meeting of the Academy of Ophthalmology, Rhinology, and Oto-laryngology in New York, 1909. The text opens with a section on Topographical Anatomy, comprising sixty-eight pages and all the illustrations but one, while the remaining pages are devoted to Clinical Considerations, and contain the solitary diagram of a defect in the visual field of a casual patient who passed out of observation and whose subsequent history is unknown, the only intimation given being that there was a true etiological connection between her accessory sinus disease and the visual disturbance. At the last meeting of the American Laryngological Association Dr. Lewis A. Coffin, of New York, in reporting some cases illustrating ocular affections due to intranasal and accessory sinus disease, presented nine diagrams of visual disturbance the histories of which he detailed.

Onodi describes thirty-eight varieties in the anatomical relation of the optic nerve to the posterior ethmoidal cell and to the sphenoidal sinus, classed in twelve groups, illustrated with thirty-five clear-cut normal-sized sections of the natural subject in varied directions. He then takes up in detail, and similarly illustrates, the bony wall of the optic canal and of the optic sulcus, dehiscence in the walls of the sinuses, the semi-canalis ethmoidalis, the partition between individual sinuses, and the turbinate bone cells.

The clinical considerations, while acknowledged still defective, comprise the visual disturbances caused by mechanical and traumatic lesions, and the various suppurations in the accessory sinuses from whatever causes. Suggestions are given as to discriminations, and a few hints as to the proper methods of operative procedure when surgical interference is requisite. J. S. C.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Disseminated Caseating Tuberculosis of the Liver in an Adult.—Thayer (*Johns Hopkins Hosp. Bull.*, 1911, xxii, 146) reports an unusual case of disseminated caseating tuberculosis of the liver in an adult. The patient was a colored woman, aged forty-nine years, who suffered from indefinite abdominal pains for over eighteen months, associated with fever, emaciation, and night sweats. The lungs showed no definite change. The liver became progressively larger, was firm and tender, and the surface was slightly irregular. There was marked secondary anemia, without essential leukocytosis. At one time there was jaundice, lasting for about a week. At autopsy, the liver was found much enlarged, covered with adhesions and studded with caseating and excavated tuberculous nodules. The enlarged liver was the striking feature of the case clinically, so much so as to suggest the possibility of neoplasm. Thayer regards the observation of interest as demonstrating "that disseminated caseating tuberculosis of the liver in an adult may be associated clinically on the one hand with appreciable jaundice, and on the other, with hepatic enlargement sufficient to form the most striking feature of the clinical picture."

The Formation of Calculi in the Body.—H. Schade (*Münch. med. Woch.*, 1911, lviii, 723) discusses the laws governing concrement formation in the body in general, and comes to the following conclusions as to the results of observation and experiment. The commonest method of stone formation is that of stratification. The origin of such calculi is intimately associated with the precipitation of colloids. Cer-

tain colloids, such as fibrin, are especially adapted to form layers or coatings, If a freely suspended body exists as a nucleus, the layers will be concentric. If crystalline substances are precipitated with the colloids, the stratification is conspicuous. The radial crystalline lines seen at times are secondary to a primary concentric layering. Of the calculi found in the human body, layer formation is usually seen in those of the urinary tract, also in salivary and pancreatic calculi, and in the calcium-bilirubin gallstones. Concrements which are largely colloidal, such as the prostatic and arthritic, are also lamellated. Cholesterin stones form an exception; inflammation is not necessarily present, inspissation from stagnation being sufficient to form them. The colloidal constituents of stones should be kept in mind in all non-operative therapeutic measures.

Spastic Constipation and Antiperistalsis.—G. Boehm (*Deutsches Archiv f. klin. Med.*, 1911, cii, 431) has made a radiologic study of several cases of spastic obstipation with reference to antiperistalsis. After reviewing Cannon's experimental work on rabbits, wherein antiperistalsis from the transverse colon to the cecum was described, he discusses the radiologic studies in man. Here the cecum was found to show bismuth shadows four and one-half to six hours after a bismuth meal. They gradually grew larger and projected down into the pelvis. In patients suffering with chronic constipation he found that in the transverse colon the fecal mass was broken up into small lumps at a well-defined ring, and it is from this ring that he feels the antiperistaltic waves arise. In rabbits he succeeded in relaxing the ring by giving atropine, but in man the drug was without apparent effect.

The Serum Diagnosis of Trichinosis.—H. Ströbel (*Münch. med. Woch.*, 1911, lviii, 672) has made use of the method proposed by Merkel to obtain trichina embryos free from muscle fibers. The infected muscle is digested in hydrochloric acid and pepsin; after solution is practically complete, centrifugalization throws down the embryos. The antigen is now prepared by digesting the worms in sodium hydrate or in antiformin. The solution is not permanent, but may retain its activity for about two weeks. The dried embryos may be preserved almost indefinitely. Using antigen prepared in this way, Ströbel was able to demonstrate fixation of complement in part of a small material. The antibodies are not demonstrable within two weeks, but exist in the serum after ten weeks. Indeed, Ströbel has obtained fixation of complement in one case one and one-half years after an attack of trichinosis. The reaction appears to be specific, but its value as an early diagnostic sign has not been shown.

The Demonstration of Tubercle Bacilli in the Urine.—R. Bachrach and F. Necker (*Wien. klin. Woch.*, 1911, xxiv, 419) consider smegma bacilli and large quantities of pus in the urine the two chief obstacles to the demonstration of tubercle bacilli. They discuss only the latter. When pus is abundant, it is often difficult to find the bacilli in stained smears unless the organisms are very abundant. The antiformin method they find helpful in such cases. Löffler's modifications of the

method of Uhlenhuth and Xylander has given the best results. The urine is allowed to settle in several conical glasses to obtain sufficient material. Twenty cubic centimeters of the sediment are mixed with an equal quantity of 50 per cent. antiformin and boiled. To 22 c.c. of the cooled fluid add 3 c.c. of a mixture of one volume of chloroform and nine volumes of alcohol, shake thoroughly, and centrifugalize. The sediment containing bacilli, if present, forms a layer above the chloroform. The supernatant fluid is poured off and the sediment *in toto* is transferred to a glass slide and fixed with albumin-glycerin fixative. It is then stained in the usual way for tubercle bacilli. In the case of mixed infections, the antiformin methods permit one to destroy all but the acid fast bacilli and thus to obtain material suitable for animal inoculation when desired. Weaker solutions of antiformin, acting at room or body temperatures, should be employed in obtaining material for inoculation into guinea-pigs, since Löffler states that the tubercle bacilli are not viable after being treated by his method.

On the Presence of "Heart Failure Cells" in the Urine.—E. Kohler (*Wien. klin. Woch.*, 1911, xxiv, 636) has confirmed the work of Bittorf, who demonstrated cells in the urinary sediment of patients with chronic passive congestion resembling the heart failure cells of the sputum. In 40 patients with chronic passive congestion, Kohler found "heart failure cells" in the urine of 24. All had marked stasis of long duration. In 21 of the cases, free erythrocytes were found; in 12 cases, free pigment, and in 21 of the cases diffuse yellow staining of the cells. The appearance of many of the altered red cells suggested to Kohler that the phagocytosis was recent and this was confirmed by his failure to obtain the Berlin blue reaction. In 7 of 8 cases of renal hematuria, similar cells were, however, found and free pigment as well. "Heart failure cells" in the urine are not, then, diagnostic of chronic passive congestion.

An Experimental Study of the Etiology of Scarlet Fever.—G. Bernhardt (*Deut. med. Woch.*, 1911, xxxvii, 791) makes a preliminary report on a study of the etiology of scarlet fever. As experimental animals, he employed the following species of lower apes: Macacus rhesus, Macacus cynomolgus, Cercopithecus griseus, Cercopithecus fuliginosus. Assuming that the scarlatinal virus, like that of smallpox, possesses a special affinity for epithelium, Bernhardt selected as inoculation material the thick, white, easily removed coating of the tongue of scarlet fever patients just before the appearance of the "raspberry tongue." The material contained, of course, numerous saprophytes and pathogenic organisms, especially streptococci, in addition to the hypothetical scarlatinal virus. The tongue scrapings were rubbed in mortars with salt solution and some of the emulsion injected subcutaneously in the groin of the experimental animal. Part of the emulsion was also placed in the animal's mouth, minute lesions of the mucosa having been made as portals of entry for the virus. There was a rise of temperature, and, between the third and fifth days, glands were removed from the groin on the side opposite to that injected, emulsions prepared from the glands and injected into healthy animals. By the third passage material was obtained which was sterile

with the known cultural methods and did not cause sickness when injected into white mice. An emulsion of this sterile gland, injected into a healthy ape, produced fever up to 39.9° C. after four days and general glandular enlargement. The tongue was heavily coated and there was erythema of the skin of the face, neck, and shoulders. The next day the skin all over the body began to desquamate, the tongue assumed the raspberry appearance, the temperature was 34.5° C. In subsequent days the skin desquamated in large scales and the animal made a good recovery. Bernhardt observed the same clinical signs after injecting scarlatinal material containing streptococci, but inoculation of a pure culture of streptococci produced not even a remote resemblance to this clinical picture. Emulsions of the tongue epithelium were now passed through a Berkefeld filter and the filtrate used for inoculations. Of four animals infected, two developed symptoms like those just enumerated, strongly suggesting scarlet fever of human beings. Recently, the author has succeeded in reproducing the same symptoms by simply rubbing the emulsion on the oral mucosa of the animal. Blister fluid obtained from a patient with scarlet fever, when injected subcutaneously into a monkey, reproduced the symptoms of scarlet fever, with a glomerular nephritis. An emulsion made from the mesenteric gland of a child dead of scarlatina caused scarlatinoid symptoms in six days in the animal, which, however, died of septicemia on the thirteenth day. In all, Bernhardt has made nineteen inoculations, and in fourteen of the animals he has observed symptoms like those of scarlet fever. Finally, in the lymph glands of human and experimental material, the author has seen inclusions which closely resemble trachoma bodies. His conclusions follow: (1) In the initial coating of the tongue, in the lymph channels of the skin, and in the lymphatic glands of scarlet fever patients a virus is present which, when injected into lower apes, after a variable incubation time, may produce a disease which resembles scarlatina of man in all essential points. (2) The virus, in the absence of bacteria, is capable of causing the same disease in other apes. (3) The portal of entry may be the oral cavity. There need be no lesion of the mucosa. (4) In all probability the virus is filterable.

A New Method of Percussing the Lung Apices.—J. Plesch (*Deut. med. Woch.*, 1911, xxxvii, 825) proposes a new method of percussing the apices of the lungs. The first rib encircles one-half of the lung apex and, with the sternum and first cervical vertebra, forms the superior thoracic aperture. Anteriorly, the lung apices extend $1\frac{1}{2}$ cm. above the first rib, while posteriorly the rib is $\frac{1}{2}$ cm. above the lung. The first rib is directly attached to the manubrium sterni; the articulation is broad and, in most cases, direct, whereas the second rib articulates with both the manubrium and corpus sterni. Therefore, when the manubrium sterni is percussed, the vibrations are transmitted throughout the first ribs, and, since the latter are in apposition with the apices of the lungs, the apices resonate. Thus, in percussing the manubrium, one obtains the mixed percussion note of both apices. If, now, one places a hand on one apex while the manubrium is percussed, the percussion note obtained is that of the free apex. In Plesch's method, the left hand is placed over the infraclavicular space close to the clavicle

and with the middle finger of the right hand the manubrium sterni is lightly percussed. The upper edge of the sternum (incisura semilunaris sterni) should be the part percussed, since it possesses a scanty covering of soft parts, even in adipose individuals. Naturally, the force of percussion stroke must be equal in comparing the two sides. To eliminate the sound from one apex, it is not necessary to exert very strong pressure with the hand. Indeed, it is sufficient to press the finger tips of the left hand into the first intercostal space. One of the advantages of this method of percussion is that the percussion note is uninfluenced by the relative muscular development of the two sides. Again, Plesch says, a lesion in any part of the apex alters the note, since the whole apex is percussed with one stroke. It is particularly in very early cases of tuberculosis that the method is of value; with bilateral apical disease it is less helpful. Plesch recommends this method as an adjuvant to the present methods of percussing the apices.

On Vertebral and Left-sided Paravertebral Liver Dulness.—P. Grocco (*Wein. klin. Woch.*, 1911, xxiv, 667) describes an area for percussing the liver which is not mentioned in the text books on physical diagnosis and is apparently new. It is generally recognized that the upper border of liver dulness begins posteriorly at the tenth intercostal space and extends from the middle line around the thorax to the right, crossing the midsternal line and ending midway between the left parasternal and mammillary lines. Grocco finds that the upper border of absolute liver dulness also crosses the posterior middle line, and normally extends $3\frac{1}{2}$ to 5 cm. to the left of it. In childhood it extends relatively farther to the left than in adults. In case the liver or its left lobe becomes enlarged, the upper border of absolute liver dulness may extend 7 to 10 or even 12 cm. to the left. Grocco has demonstrated the left-sided dulness posteriorly in over 300 examinations and also by Röntgen ray studies and postmortem findings. To demonstrate the dulness, one percusses from above downward along the right paravertebral line, then along the spinous processes, and finally to the left of the vertebræ, marking the points at which pulmonary resonance ceases and liver dulness begins. Then, beginning well outside the left scapular line, one percusses toward the vertebræ, working along the line of dulness, to determine the extent of hepatic dulness to the left. This is measured. There are many useful applications of this procedure. By means of it Grocco diagnosticated a small abscess of the left lobe which gave no other physical signs. In determining whether dulness at the right base is pulmonary or hepatic in origin, a comparison of the level of dulness on either side of the vertebræ is usually conclusive.

Experimental Measles in the Monkey.—J. F. Anderson and J. Goldberger (*Public Health Report, U. S. Mar. Hosp. Serv.*, Washington, 1911, xxvi, 887) have added a supplemental note to their recent report on experimental measles in the monkey (*Ibid.*, 1911, xxvi, 847). They have inoculated defibrinated human blood, obtained within thirty-two hours after the eruption of measles, into rhesus monkeys. The inoculations were intraperitoneal, subcutaneous, intracerebral, or intravenous. In certain of the animals they obtained well-

defined febrile reactions accompanied at times by macular or maculopapular skin eruptions of short duration (two to three days). From animals exhibiting febrile reaction they have withdrawn blood and inoculated other monkeys and have adduced evidence of transmission of the virus through three generations. The susceptibility of the rhesus monkey appears not to be very great and is subject to considerable individual variation. The time interval between inoculations and febrile reactions was five to seven days. The bloods used for inoculation gave no visible growth in standard glucose broth in fermentation tubes.

The Third Heart Sound and the "B" Wave in Slow Heart Action.—J. D. Windle (*Quart. Jour. Med.*, Oxford, 1911, iv, 284), in a study of the third heart sound and the *B* or *L* wave arrives at the following conclusions: (1) A third heart sound with an associated *B* wave was present in 2 out of 193 observations on normal individuals. The pulse rate was abnormally slow and sinus irregularity present in both cases. (2) In 13 instances of the number of persons examined, a decided *B* wave was present in the venous tracing, in none of which was a third sound heard. Marked sinus irregularity was present in 9 of the records. The pulse rate in these cases varied from 50 to 60 per minute. (3) When the pulse rate was quickened in cases in which the *B* wave was persistently present under normal conditions, it did not show in the tracing when the pulse rate exceeded 80 per minute. When associated with sinus arrhythmia it was absent from the venous curve when the arrhythmic beats approached this rate. (4) The *B* wave may first appear in the venous tracing coincidently with regular slowing of the heart to a rate of from 50 to 70 per minute under digitalis. This may be brought about in the normal heart. In no case observed was there a third sound present. In slowing resulting from partial heartblock due to squill, an extra wave succeeding blocked auricular waves is shown to occur coincidentally with the establishment of heartblock; in this case a clearly marked third sound was present. (5) Venous curves showing the *B* wave may present a close resemblance at times to those resulting from extrasystoles or cases of heart block. (6) With a certain rate of pulse the *B* and *A* waves may fall together and give an appearance to the curve closely simulating an increased *a-c* interval.

The Bacteriology of the Sputum from the Lower Respiratory Tract.—Hastings and Niles, (*Jour. Exper. Med.*, 1911, xiii, 638) have investigated the bacteriology of the sputum from the respiratory tract taken below the epiglottis, using all precautions to avoid mouth contamination. They studied 183 cases, making 341 cultures in all, over a period of seven years. They found a marked change in the incidence of various bacteria from year to year, but in the sum total, the micrococcus catarrhalis was the organism in 21 per cent., the aureus and streptococcqs coming second and third before the pneumococcus. There were numerous cases of lobar pneumonia, especially with atypical signs, where the pneumococcus was not found at all, and they feel sure that pneumonia may be caused by other bacteria. Only 38 per cent. of the infections of the respiratory tract below the glottis are pure. While in a large precentage of cases the micrococcus catarrhalis is a secondary invader, it may assume pathogenic properties,

SURGERY

UNDER THE CHARGE OF

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Concerning the Experimental Production of Gastric Ulcers through Nerve Lesions.—KAWAMURA (*Deut. Zschr. f. Chir.*, 1911, cix, 540) says that the pathogenesis of stomach ulcers is still in the dark, notwithstanding the numerous investigations which have been made. Kawamura has studied the subject from the side of the nervous influence, and has experimented on dogs and rabbits. That stomach ulcers can arise from disturbances of the nervous system has been shown experimentally by many workers. In dogs after section of the vagus, extirpation of the celiac plexus including the celiac ganglia, etc., the findings in the stomach were always negative, while in rabbits various changes were found, such as hemorrhages, erosions, ulcerations, and scars. In one rabbit's stomach, which was extirpated a few hours after operation, there was observed a typical round ulcer at the junction of the pylorus and duodenum. There were found many times, besides ulcers at the pylorus, hemorrhages or hemorrhagic erosions in other places. Further, there were observed streaky or star-shaped scars in the mucous membrane of animals which died some days after the operation. In one dog killed seven days afterward there was observed a bean-sized typical ulcer in the pyloric region of the stomach. Also in animals in which the intestines were merely moved about, or in which colleagues had performed a nephrectomy, or decapsulation of the kidney, similar anatomical lesions were found in the stomach. Hemorrhages and hemorrhagic erosions were found even in animals which were apparently sound. Ulcerations of the stomachs of rabbits may be produced, therefore, from vagotomy or from extirpation of the celiac plexus, including the celiac ganglia. In further investigations along these lines, dogs should be chosen because the results in rabbits are ambiguous. In the urine of the animals experimented on no abnormal elements were observed which could stand in a causal relation to the extirpation of the celiac plexus and celiac ganglia. After vagotomy the hydrochloric acid was always diminished. After removal of the celiac plexis it was sometimes increased, sometimes diminished.

Pantopton-scopolamin Injection Narcosis.—KRAUSS (*Zentralbl. f. Chir.*, 1911, xxxviii, 697) reports the results of 57 injection narcoses, some with and some without the application of a tourniquet to the

extremities. In the 33 cases in which the tourniquet was employed, the constricting bandage was applied to three extremities, the two lower and one upper, and fifteen to twenty minutes later the pantopton-scopolamin was injected. In all cases the operation was begun three-quarters of an hour to one hour after the injection. The earliest termination of the narcosis was thirty minutes after the injection. In 34 cases the operation was completed without the administration of ether or chloroform, 15 with and 19 without the application of the tourniquet. Most patients were restless when the skin incision was made, and remained so during the whole operation. Frequently there was severe pain. Only 6 patients were completely quiet. Radical operations were performed for small herniæ, excision of bursæ and ulcers, resection of ribs, and unilateral strumectomies. Krauss was impressed with the thought that local anesthesia would have given better results. Ether or chloroform was necessary in 23 cases, in large amount in some cases. The availability of this method is limited, because of the difficulty of operating at just the proper time, which must be determined beforehand, at the time of the injection.

Appendicitis and Pregnancy.—Schmid (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, xxiii, 213) made a study of 28 cases from the clinics of v. Eiselsberg and Chrobak, v. Rosthorn, and 486 others collected from the literature, with particular reference to the complications which may arise from appendicitis in the pregnant woman. The occurrence of appendicitis in the pregnant woman is relatively frequent. About 2 per cent. of all cases of appendicitis in women are found in association with pregnancy. About 1 per cent. of all pregnancies are associated with appendicitis. Pregnancy itself does not seem to favor the first attack of appendicitis, but rather a recurrence. The causal relationship is not clear. Mild cases of appendicitis (with and without operation) run about the same course with or without pregnancy. Severe cases are usually deleteriously influenced by the interruption of pregnancy (by abortion or normal delivery). The pregnancy in a large number of cases will be terminated before the normal time, owing to the involvement of the peritoneum. Appendicitis can cause involution disturbances, the formation of adhesions, sterility, habitual abortions, extra-uterine pregnancy, and probably can also favor hyperemesis gravidarum. The diagnosis of appendicitis during pregnancy, delivery, and the puerperium is usually not easy. The prognosis is generally unfavorable. The explanation for this is to be found not so much in the pregnant condition as in its termination by birth or abortion on the one hand, and in the deferred diagnosis and therefore the delay in carrying out the proper treatment. Only in mild cases is the conservative treatment to be advised, and then only when the patient can be carefully watched. In other cases operation is to be advised, and it should be done as early as possible. In the intermediate stage operation should be done immediately rather than to wait for a free interval as in non-pregnant women. The artificial termination of pregnancy should not be regarded as the only treatment. When there are no signs of beginning labor, appendectomy is to be performed as in non-pregnant women, although the incision should be made as far laterally as possible and the uterus should be disturbed as little as possible.

After the operation the administration of opiates is indicated. When termination of the pregnancy is threatened and when peritonitis is present, after appendectomy and provisional closure of the abdominal cavity, the uterus should be emptied (by forced dilatation or Cesarean section), and then after again exploring the abdominal cavity the final drainage should be placed.

A Method of Replacing the Excised Rectum by a Portion of Small Intestine, with the Avoidance of Gangrene.—Helsingsfors (*Zentralbl. f. Chir.*, 1911, xxxviii, 728) says that in the operation for the removal of a cancer of the rectum and the avoidance of an artificial anus by bringing down the upper cut end of the bowel to the site of the sphincter ani, the great danger is gangrene. This is due to the disturbance of the blood supply of the portion of bowel thus mobilized. Helsingsfors overcame this danger by the following operation: After exposure by the Kocher coccygeal method, the rectum was separated, and after opening the periotneum an effort was made to mobilize the rectum sufficiently to permit the reëstablishment of the intestinal passage through the intact anal portion. This was rendered very difficult by the shortness and tension of the pelvic mesocolon. Passing the hand through the opening in the peritoneum, a long and movable colon-sigmoid loop was recognized and brought out of the wound. It was evident that this could be brought down without the least tension to the anal opening. Further separation of the rectum was deferred, and it was divided between two ligatures. The edges of the upper cut end were turned in and the lumen closed by a few serous sutures without difficulty. The rectum was then freed to the anal portion and removed just above the latter. After excision of the anal mucous membrane, the apex of the loop of colon-sigmoid was drawn out through the anal opening and fastened to the anal skin by a few sutures. The wound was cared for in the usual way and the gut opened in the anal opening. The after-course was unusually favorable, and defecation occurred through the continent anus from the beginning. Since the mesentery of the bowel drawn down was uninjured, gangrene was impossible. The healing was very favorably influenced by the contact of the intact serous surfaces. Investigations on 22 postmortems showed that in 19 the mesentery of the colon-sigmoid was long enough to permit this operation to be performed. In 3 cases, in consequence of inflammation of the mesentery, this was so shortened that the operation would be impossible.

Further Experiences with Anesthesia by the Intratracheal Insufflation of Air and Ether.—Elsberg (*Annals of Surgery*, 1911, liii, 749) says that it is always advisable to anesthetize the patient in the ordinary way by inhalation before the intratracheal tube is introduced, because it is unpleasant for the patient to have the tube inserted into the trachea while he is conscious. Besides, the beginning of insufflation of the air and ether mixture while the patient is conscious is almost certain to give a good deal of spasmodic coughing. It is also advisable to give the patient a small dose of morphine hypodermically before the operation, so as to reduce the reflex irritability of the larynx. While it is easy to kill a dog with ether given by inhalation, it has been found

impossible to kill it by intratracheal insufflation. In human beings the experiences have also been very satisfactory, and so far it seems that it is impossible to give a patient too much ether by Elsberg's apparatus. If the full amount possible is insufflated, it means that more ether escapes by the side of the intratracheal tube and out of the larynx and mouth. Up to the present time Elsberg anesthetized close to 100 patients by means of intratracheal insufflation. Operations of the most varied kind were performed on different parts of the body. He has not seen a single untoward symptom during or after anesthesia. During the anesthesia the patient remains pink, the breathing slow and superficial, the pulse is slightly accelerated. The rate of the pulse can often be controlled by the anesthetizer, if the cardiac oscillations of the mercury column in the manometer are marked. He had only one patient in whom complete anesthesia could not be obtained by the insufflation. Vomiting is rare after ether anesthesia by intratracheal insufflation, and Elsberg has never seen any patient vomit during the course of the anesthesia, neither has he seen any unpleasant after-effect from it. None of the patients were hoarse or complained of laryngeal symptoms, nor were any pulmonary symptoms observed. The anesthesia is very useful in operations upon the neck, such as thyroidectomy. In the first place the anesthetizer is away from the field of operation. More important, the operator can manipulate the trachea as much as necessary without causing disturbance in breathing or interference with the anesthesia. Nor need he fear a sudden collapse of the trachea in the course of the removal of a large goitre. The presence of the tube in the trachea will guard against such complications. There is no danger of aspiration of blood into the lungs in operations upon the mouth and tongue, and tamponnade of the larynx is unnecessary. The current of air which is continually flowing upward in the trachea by the side of the tube will blow out all of the blood which tends to run down into the larynx and trachea.

A Study of a Case of Cystic Ureteritis.—Augier and Lepoutre (*Ann. d. mal. d. org. gén.-urin.*, 1911, i, 880) says that there exists a category of cysts of the ureter, the structure and connections of which show that they are of epithelial origin and that they come from the epithelial lining of the ureteral mucosa. The lesions which accompany the production of these cysts involve all the layers of the ureteral wall. The lesions of the adventitia, muscularis, and submucosa, are the result of an inflammatory process which is accompanied by a cellular infiltration of the different tunics, or at a more advanced stage by a distinct sclerosis. The epithelial lining is deficient at many points. Where it is preserved it is the seat of proliferation resulting in epithelial papillæ projecting into the lumen of the duct or gland like invaginations, epithelial crypts and buds, which invade the submucosa to a variable depth. A certain number of these buds become channelled by a cavity which opens on the surface of the interior of the ureter by a canal more or less straight. Others remain included in the thickness of the submucosa and lose all relation with the epithelial surface. These epithelial masses in a certain number become the seat of proliferation which ends in the formation of microscopic cysts included completely in the wall of the ureter without any communication with the lumen.

As they enlarge they are covered by the layers of the ureteral wall. At a later stage they become enucleated from the ureteral wall and are then completely within the lumen of the tube, to the wall of which they remain attached only by a pedicle. Some of the cysts, being arrested at a certain stage of their development, may remain included in the ureteral wall itself. These cysts are made up of a thin external layer of connective tissue upon which is laid an epithelial layer formed of epithelial elements, cuboidal, polyhedral, or elongated, which conform absolutely to the epithelial elements of the modified ureteral mucosa. The epithelial origin of these cysts, therefore, can not be disputed. Their formation is preceded and accompanied by profound lesions of the ureteral mucosa under the influence of an irritative or inflammatory process.

Mobile Cecum, Fixed Appendix, Perityphlitis.—Sick (*Zentralbl. f. Chir.*, 1911, xxxviii, 759) refers to a condition which he has frequently observed during the past two years in from 70 to 80 cases seen each year. He regards it as of etiological importance in a large number of cases of perityphlitis. Frequently the length of the mesocecum was disproportionate to that of the meso-appendix. Either the meso-appendix was disproportionately short, frequently also cicatricial and changed to a cord-like structure; or the appendix itself was fixed tightly in one of its usual situations, so that it presented a fixation band for the cecum. In typical cases of this kind, the appendix was so stretched that it was difficult to see or feel where it ended. Sometimes only a part was so fixed and the junction of the fixed and movable portions was kinked, and not rarely the site of an acute inflammation. Often the junction of the cecum and small intestine was so blocked as to interfere with the passage of gas and feces. Frequently there was found a tendency to torsion, which is to be explained by the fixation of the appendix, a condition resembling a long sigmoid loop with a narrow base being produced. Torsion of the cecum occurs with characteristic symptoms. Sick says that the few genuine cases of volvulus which he has seen were not due to this mechanism, but to an abnormally long mesentery. While the condition may be of mild grade in one attack, the next attack may be of the streptococcic, phlegmonous variety.

Pyelotomy for the Removal of Renal Calculi.—Bazy (*Ann. d. mal. d. org. gén.-urin.*, 1911, i, 769) says that most renal calculi can be removed by an incision made only in the pelvis of the kidney, without involving the renal parenchyma and without disturbing the functional value of the kidney. It will therefore be useless to undertake, preliminary to operation, methods of investigation to determine the functional value of the kidney, which may be painful and poorly tolerated by the patient, and may sometimes be dangerous. The operation can be done on all patients capable of tolerating an operation of moderate duration and minimum gravity. It is suitable, therefore, for cases in which the opposite kidney is affected and where the kidney to be operated on is the better of the two and should be treated with care. These conditions were present in two of Bazy's cases, the patients being exhausted by suffering and suppuration. The operation can be employed in cases in which the pelvis is infected. Union by first inten-

tion does not seem to be hindered by this complication. One can recognize in advance by a study of skiagraphs whether a pyelotomy or nephrectomy should be done. The operation is so benign that it ought to be done early, as soon as the diagnosis is clearly made.

THERAPEUTICS

UNDER THE CHARGE OF

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Nerve Recurrences as a Result of Salvarsan Therapy.—Benario (*Münch. med. Woch.*, 1911, lviii, 732) has collected from the literature 126 cases of symptoms referable to the cranial nerves that have occurred in at least 1400 cases of syphilis treated with salvarsan. Of these 126 cases he excludes 8 as cases of latent syphilis, tertiary syphilis, or parasyphilis. Of the remaining 118, 5 patients were in the first stage, 22 in the combined primary and secondary stages, 82 in the secondary, and 9 not accurately classified but very probably secondary. Benario thinks that the small number of nerve recurrences occurring in primary affections, compared with the total number of nerve recurrences, shows that salvarsan does not appear to be the cause of the recurrences. This is especially true because the number of primary affections treated with salvarsan is evidently very great. The nerves affected were the optic, oculomotor, trochlear, trigeminus, abducens, facial, and auditory. In 30 cases, or 26.1 per cent., the recurrence occurred in the first month after the injection; in 46 cases, or 40 per cent., in the second month; in 27 cases, or 23.5 per cent., in the third month; and in 8 cases, or 7 per cent., in the fourth month. Benario believes that these nerve recurrences are not due to a toxic action of salvarsan, but are clinical symptoms of a swelling induced by the pathological process. He gives the following reasons for this belief: (1) The interval between the injections and the onset of the nerve manifestations is considerable. (2) The cause of the recurrence seems to be an irritation or inflammation of the nerve, as is particularly shown in the affections of the optic nerve. On the contrary other arsenical preparations seem to cause an atrophic condition of the nerves. (3) The recurrences seem to appear almost exclusively during a certain period of syphilis. (4) Such recurrences have not been observed in non-specific diseases treated with salvarsan. (5) These recurrences are cured by specific treatment, particularly by renewed treatment of salvarsan. (6) The recurrences appeared in most cases after the smaller doses of salvarsan. (7) These same symptoms have been observed under mercurial treatment. Benario found that certain groups of specific disease were more prone to nerve manifestations. These recurrences occur mostly in the recent secondary stage. Certain specific lesions seem more inclined

to result in nerve recurrences than others. Benario observed that chancres about the head were particularly inclined to do so. Such initial lesions seem to institute a more severe variety of syphilis, and the closer relation between the initial lesion and the central nervous system may be an important factor in the production of these recurrences. He also noticed that nerve symptoms recurred more often in cases with the marked skin eruptions especially of the papular variety. Patients with headache were also more prone to nerve recurrences. Therefore he advocates that these groups of cases should have a more intensive treatment with salvarsan as a prophylactic measure. Alcohol and tobacco should be forbidden after salvarsan therapy, because alcohol and tobacco habitués are more prone to nerve affections in syphilis. Certain prodromal symptoms may indicate a nerve recurrence, such as headache, dizziness, ringing in the ears, or some disturbances with vision, and patients should be instructed to report for further treatment in the advent of any such symptom. Benario adds that these nerve recurrences have been more carefully noted since salvarsan therapy, but that probably they have occurred as frequently under former methods of treatment. He supports this view by some statistics.

The Principles of Internal Treatment with Iodine in Combination with Fatty Acids.—Loeb and van der Velden (*Therap. Monats.*, 1911, xxv, 209) say that lipoiodin from a theoretical standpoint is the best of the many combinations of iodine and the fatty acids—such as sajodin, iodifin, and iodidol. Lipoiodin is gradually absorbed and is eliminated much slower than other similar preparations, and thus secures a more permanent deposit of iodine in the body tissues. The remedy seems to have an especial affinity for nerve and fat tissues. It is well borne by the stomach, and does not produce the symptoms of iodism, although its therapeutic effects are well marked.

Vaccines in Puerperal Sepsis.—Walters and Eaton (*Bost. Med. and Surg. Jour.*, 1911, clxiv, 524) report 50 cases of puerperal sepsis treated with vaccines. They include all patients who have been treated, the good and the bad, the early and the late. A few of the patients received antipartum prophylactic injections because of bacteriological findings or unusual opportunities for possible infection. These all recovered. Others likewise received prophylactic injections that showed pure cultures of streptococcus in the uterus, post partum, but without any clinical symptoms of sepsis. Of the 50 cases reported, 4 patients died within twenty-four hours after the treatment, being practically beyond hope of recovery when treatment was instituted. Three other patients were moribund at the beginning of the treatment, but life was possibly prolonged for two or three days. Excluding these 7 cases, there were 43 patients, of whom, 41 recovered. The other 2 patients died after surgical intervention. Walters and Eaton administered a polyvalent preparation immediately after the diagnosis was determined by bacteriological tests. This polyvalent preparation was superseded by an autogenous vaccine about twenty-four hours later. No injurious effects or aggravation occurred as a result of the injection. Walters and Eaton do not claim that the vaccines should replace other treatment, but that they should be used to assist the other methods.

They advise, however, leaving the patient as free from manipulation or local treatment as possible. In their series of cases a hot vaginal douche usually was employed, but only in one or two instances was an intra-uterine douche used. Walters and Eaton prefer to draw no definite conclusions concerning the results of the treatment, although they think that two facts have been demonstrated by their work; one is that the treatment is harmless; the other is that patients have shown much improvement after the injections and have recovered when apparently hopeless.

The Medicinal Treatment of Hyperacidity.—Roubitschek (*Deutsch. med. Woch.*, 1911, xxxvii, 874) advocates hydrogen peroxide in cases of indigestion due to hyperacidity. Roubitschek found that fluid preparations were much more satisfactory than the solid preparations that are recommended by some. He first gives about 300 c.c. of a $\frac{1}{2}$ per cent. solution three times a day before meals. If no result is obtained from this, the strength of the solution is increased to $\frac{3}{4}$ or 1 per cent. The disadvantage of the stronger solutions is that they are apt to cause vomiting, and solutions stronger than 1 per cent. are almost sure to do this. The results were extremely good in 80 per cent. of the cases treated. The average length of treatment was fourteen days. The permanent results achieved by this method of treatment are somewhat obscured by the fact that the patients were only under observation for a period of three months after the treatment. However, during this time the patients remained free from symptoms and Roubitschek cites a case reported by Poly, who was perfectly well one and one-half years after treatment.

The Action of Fibrolysin.—Mendel (*Therapie d. Gegenwart*, 1911, lii, 155) reviews the work of other observers regarding the action of fibrolysin, together with his own personal experiences. He says that this remedy has a specific action in promoting the absorption of scar tissue of every description. He speaks particularly of its good effect in the treatment of arthritis deformans. Untoward by-effects are very infrequent. A febrile reaction occasionally results from an injection of fibrolysin, and is due, according to Mendel, to anaphylaxis. Mendel suggests that fibrolysin may be given in the form of suppositories in suitable cases.

The Treatment of Cancer with Body Fluids and Cancerous Ascitic Fluid.—Risley (*Jour. Amer. Med. Assoc.*, 1911, lvi, 1383) reports the work done at the Massachusetts General Hospital on the treatment of inoperable cancer with various normal and abnormal body fluids and with cancerous ascitic fluid. Forty-five patients were treated by these injections; most of them were treated with ascitic fluids obtained from patients suffering from cancer. An effort was made to obtain ascitic fluids from patients resistant to their disease, with the idea that the amount of antibodies in these cases would be larger than in very active or non-resistant cases. A second smaller group of cancer patients was treated with various normal and abnormal body fluids for purposes of control. Finally, untreated patients were observed coincidently for the purpose of comparison with the treated cases. Risley gives briefly

the definite results witnessed in this series of cases. In 5 cases there was a decrease in, or absolute abolition of, the pain previously complained of. Increase in pain was experienced in 2 cases. In 3 cases there was a dicided increase in the discharge from an ulcerated surface and a breaking down of cancerous tissue, considerable portions of which sloughed away entirely—enough to cause a moderate hemorrhage. Moderate increase in the discharge from an ulcerated surface has been noticed in practically every patient treated. This in some cases was only temporary, but was followed later by a noticeable cleaning-up of the ulcer and more healthy granulations. Cessation of bleeding in several cases of uterine cancer was seen. There was an apparent retardation of the growth in 8 cases for periods of two to five months, and in 3 others for a period of over one month. Twelve patients have remained in excellent general physical condition, gaining strength and weight in spite of a slowly growing process. On the other hand, in no case was there actual shrinking in the size of the tumor, and in 2 cases there seems to have been a decided increase in the rate of the growth of the tumor. In no instance was any marked harm done. A local and constitutional reaction has occurred more often from the injection of the fluids from resistant cases, and this fact seems to indicate that their action is more specific. Risley draws the following conclusions, based on a careful analysis of the results in this series: (1) The various transudates and exudates of the body, cancerous and non-cancerous, have no effect in retarding the growth of cancer in mice. (2) The use of cancerous ascitic fluid from patients in the active or even moderately resistant stages of the disease has no permanent effect in preventing or checking the growths of cancer, or permanently benefiting the cancer patient. (3) The other non-cancerous body fluids are even more inert. (4) Temporary beneficial effects may be noticed for periods of one to five months, but the course of the disease is in no way permanently retarded. (5) Temporary relief from pain, especially in uterine cases, and in other cases in which large doses can be given, and retardation of the growth for periods varying from one to five months, may be expected in a small per cent. of the cases. (6) Noticeable benefit in the general physical condition has resulted in one patient with cancer of the ovary by the injection of her own fluid.

The Treatment of Rheumatic Diseases with Vaccines.—Ball (*Brit. Med. Jour.*, 1911, 2628, 1105) reports in detail a few cases of rheumatoid arthritis that were favorably influenced by the use of streptococcus vaccines. Ball was impressed by the peculiar sapremic appearance of chronic rheumatic cases, and in some of them it was possible to trace in the history the onset of the disease following on some distinct infection, or subsequent to a chronic suppuration. He believes, from experience with a large number of cases, that the focus of infection can at times be ascertained, and although a few are probably due to specific microörganism, many cases are due to a general sapremia following from a localized seat of infection. He has seen many cases where the focus of infection has been found microscopically to contain chiefly streptococci. In some cases even, where no seat of infection such as bad teeth, leukorrhea, intestinal putrefaction, and colitis, could be found, he has used the antistreptococcic serum with success.

So many of these cases responded with such remarkable results that he thinks their use is justified in all doubtful cases. Even in a case of acute articular rheumatism following an attack of gonorrhea with subsequent gleet, he has had success by the employment of antistreptococcic vaccines, where the injection of gonorrheal vaccines had failed.

Hexamethylenamin: A Remedy for Common Colds.—Miller (*Jour. Amer. Med. Assoc.*, 1911, lvi, 1718) has been led to prescribe hexamethylenamin for common colds by the reported excretion of this drug in the saliva and by the middle ear and bronchial mucous membrane. He says that in most cases it acts promptly and efficiently. The irritating watery secretion stops and the fever, aching, and general malaise diminish. The best results are obtained when the remedy is administered early. Larger doses of hexamethylenamin are required than when it is given as a genito-urinary antiseptic. Bladder irritation is the only ill effect of the drug, and in order to lessen this possibility large amounts of water must be taken.

The Therapeutic Action of Bile.—Inouye and Sato (*Arch. f. Verdauung-Krank.*, 1911, xvii, 185) introduce their article by a discussion of the physiological action of bile as determined by many different observers. They also relate their findings in 15 cases studied by them from a metabolic standpoint, that seem to indicate that the administration of bile in certain conditions is based upon rational therapeutics. Consequently, they advocate the administration of bile in jaundice due to various causes. They say that absorption of fat is increased by its use, and that it also has a laxative effect. They advise giving inspissated ox-bile in some sweetened aromatic water, in doses of from 0.5 to 1 gram one hour before meals. The authors say that if it is given with considerable water in this way it will not disturb gastric digestion.

Utilization of Fats and Oils Given Subcutaneously.—Mills and Congdon (*Arch. of Int. Med.*, 1911, vii, 694) draw the following conclusions form their experimental work of injecting various fats and oils subcutaneously into animals. Olive, peanut, cocoanut, sesame, cottonseed, lard oils, unsalted butter-fat, and lard may be given hypodermically and over a condiserable period without local irritation, provided aseptic care is used, and no constitutional disturbance occurs, and provided precautions are used to prevent injection into the bloodstream. Emulsions of these oils made with 3 to 5 per cent. of egg lecithin and water are permanent, and cause no irritation if given subcutaneously. Oils and fats given subcutaneously are absorbed by means of the lymphatic system, and eventually reach the thoracic duct. Lymphatic vessels and glands in contact with and transmitting oil for any length of time become hypertrophied and are thus better able to carry oil. The amount of absorption of plain oil from the subcutaneous tissues after injection during starvation is so small as to be negligible. Emulsified oils and fats injected during starvation are absorbed in amounts sufficient to furnish from one-half to two-thirds of the full calorific requirement of the animals injected. Oils and fats so injected and absorbed have no more influence on the destruction of protein in starvation than has fat given alone by mouth. Plain oils injected sub-

cutaneously under conditions of low protein ingestion are little, if any, better absorbed than when similarly given during starvation. Emulsified oils injected under these conditions are absorbed quite as well as similar oils given to starving animals. Plain and emulsified oils are absorbed about equally well when the animals injected are given a plentiful supply of protein in their food. This probably furnishes the large quantity of lipolytic enzymes necessary for body action on plain oil. The injection of oils subjected to lipolysis causes death, which is due apparently to the production of oleic or other acids with the possible formation of toxic quantities of soaps. Oil absorbed from the tissues after subcutaneous injection is (1) burned in the body for the production of heat and energy, thus sparing the body fat; (2) retained as such within the organism; or (3) possibly converted into body fat by reconstruction in the liver, from which it may be sent for storage to the various fat depositories, after which it is drawn on as needed. Proof of this last proposition is lacking. It seems likely, from comparative examination of the iodine indices of the ether extracts of visceral and adipose tissue that the actively functioning viscera use oil and fat absorbed after subcutaneous injection for the direct performance of their functions, and that the storage of the foreign fat given in excess of the nutritive requirement takes place principally in the subcutaneous tissue, liver, and lungs, to a small extent in the kidneys and spleen, while the pancreas and stomach and intestines are practically uninfluenced. This demonstration that after injection under suitable conditions oils can be absorbed to an amount capable of covering so large a proportion of the calorific requirement suggests the application of such injections to the treatment of wasting diseases, to the cachectic conditions associated with imperfect metabolic processes, and especially to tuberculosis, in which the intolerance to fats is almost symptomatic.

PEDIATRICS

UNDER THE CHARGE OF

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Prophylaxis and Therapy in Scarlet Fever.—Lange (*Deutsch. med. Woch.*, 1911, xxxvii, 913), in a clinical exposition on the prophylaxis and therapy of scarlet fever, emphasizes the point that recovery from the disease gives the only known immunity, and that no drug so far as known can do this. The immunity is sometimes only partial, and allows of a second but slight attack. Some individuals seem naturally immune. Isolation is the important factor in prophylaxis, and should be continued for at least five weeks, and longer if desquamation continues. Companions and near relatives of the patient should be isolated and carefully watched for signs of scarlet fever for at least eight days before being allowed to mingle with the community. Every case of scarlet

fever should be compelled to go to a hospital where isolation is perfect, and besides, this plan lessens the chances for spreading the disease through poor quarantine at home. The hospital treatment of all cases would reduce the number of cases to a considerable extent. Under therapy Lange gives the usual rules for isolation in the home. He does not approve of cold baths, but favors a daily cleansing bath of tepid water. Most important is the regular cleansing of the mouth, nose, and throat. This should never be too severe, and the best solution is a weak salt solution. Weak solutions of boric acid and peroxide of hydrogen are permissible. Swabs should not be used on the mucous membranes. A daily careful examination of the patient's condition by the physician himself is extremely important. A moderate milk diet is probably the best in avoiding the development of nephritis. Meat and meat extracts should not be given during the first three weeks. Food with a low salt-content is desirable. Eggs are best withheld until after the third week if no nephritis has developed. Spices of all kinds and alcohol in any form should be prohibited. It has been claimed, but not proved, that urotropin is useful in avoiding a nephritis. More important is the daily tepid bath in keeping the sweat glands active and relieving the kidneys. The use of ointments on the skin is not approved, as it tends to clog the pores, and a dusting powder is preferable to allay itching. Absolute rest in bed, even in mild cases, should be continued for at least four or five weeks in uncomplicated cases. It is preferable to have the desquamation completed before the child leaves the bed. Cool packs are sufficient to control most high temperatures, and cold baths should only be used as a last resort. The treatment in general should not be so complicated or continuous as to interfere with the patient's rest and sleep. While the results of Moser's serum for scarlet fever are praised by some and condemned by others, it must be admitted that abnormally severe forms of the disease and very toxic cases show a marked general improvement after the use of the serum which is not usually found in the same type of case not so treated. Moser's serum is obtained from the horse, after injecting the animal with living, bouillon cultures of streptococci taken from the heart's blood of children dead from scarlet fever. The influence of the serum on the complications of the disease is still doubtful. Besides the serum, the only treatment available is symptomatic. Lange mentions camphor, digalen, and strophanthin, with normal salt by the bowel, as measures toward stimulating the circulation. He suggests kallargol internally, in the form of jalon, a new preparation. In scarlet fever complicated by diphtheria, Lange has used, with good results, the Heubner-Taube method, injecting 5 grains of a 3 per cent. solution of carbolic acid into the peritonsilar tissue on both sides, twice daily. In nephritis, when hot packs fail in their result, he employs pilocarpine.

Taxis and Succussion; A New Treatment of Intussusception.—John Zahorsky (*Archives of Pediatrics*, 1911, xxviii, 380) has devised a mechanical method of treatment for intussusception which he calls "the combined taxis and succussion method," and which is always to be preceded by a rectal injection of water to obtain the best results. The method is as follows: After the child is anesthetized, the abdomen is bared and the hips raised by a small pillow. The tumor is grasped

through the abdominal wall and firmly compressed for a few moments in order to reduce the swelling. Then the thighs are flexed on the abdomen, knees or legs grasped, and with a rapid up and down movement the lower part of the trunk is vigorously shaken for several seconds. The tumor is grasped again and compressed, and while pushed against any part of the posterior abdominal wall, the fingers push or strip the intussuscipiens out of the intussusceptum, the fingers at the same time making a trembling motion which assists in the reduction. After a few minutes of taxis the succussion is again resumed, and these efforts successively alternated. Sometimes, because of the mobility of the mass, taxis is not effective, and reliance must be placed entirely on the succussion or shaking. In all cases noted the tumors disappeared while the shaking was being done, although taxis had diminished the size of the swelling. There may be two reasons for this—either the loosening of adhesions by the sudden jarring, or preferably, that when a downward movement is suddenly arrested the resulting force is strongly outward, and if the invaginated mass is situated near the median line, the afferent and efferent parts of the intestine have a tendency to go away from the centre and thus pull the invagination apart. If the diagnosis of intussusception has been prompt, the method should be given two or three trials of fifteen minutes each, at intervals of two or three hours, before resorting to surgical treatment. However, the success of the new method of treatment is unlikely, if there is much swelling and local contraction. In the reports of three cases given, it is clearly demonstrated that succussion carefully used is a powerful means of reducing intussusception; but for the best results, this must be undertaken by one thoroughly practised in the technique.

The Blood Pressure in Cases of Acute Nephritis of Children.—Lennox Gordon (*Archives of Pediatrics*, 1911, xxviii, 343) states that in cases of acute nephritis occurring in young children the blood pressure is raised, and often raised to a marked degree. This fact has apparently not been recognized by authorities on children's diseases. It is extremely difficult, in small children, to determine variations in pulse tension by digital compression, but with the sphygmomanometer any change which may occur is easily noted, and the fact that the sphygmomanometer has been very little used among children will explain why so little change in blood pressure has been found in nephritis. Before determining whether the blood pressure was raised or lowered, the normal pressure for children at different ages had to be determined. This was obtained by working out the averages on a series of 170 cases between the ages of a few months and twelve years. Observations were then made on 9 cases, 7 of which were cases of acute nephritis, and 2 were chronic, with acute symptoms superadded. From the results obtained in these cases the following conclusions were drawn, namely, that in children suffering from acute nephritis the blood pressure is raised, and that this rise may be very great. In 3 out of the 7 acute cases the hypertension was very marked. This fact is of diagnostic value, as in no other disease of childhood is there to be found the same high range of blood pressure. Those cases having the highest pressure were those in which only a trace of edema was noticeable, and also it was noted that in these same cases the quantity of blood in

the urine was very great; the explanation being, probably, that the greatly increased blood pressure had caused a rupture of the renal capillaries. It is difficult to explain the high tension and rapid drop which occurred in some of the cases, except by assuming a large degree of spasm due to some toxin acting on the arterial walls. The fact should be emphasized that in children it is only by means of the sphygmomanometer that changes in the blood pressure can be accurately ascertained.

OBSTETRICS

UNDER THE CHARGE OF

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Stroganoff's Treatment of Eclampsia.—Roth (*Archiv f. Gynäkologie*, 1910, vol. xci, Part 2) has employed this treatment of eclampsia in 31 cases in the clinic at Dresden. It consists in giving morphine, chloralhydrate, and chloroform, by a definite routine, to prevent the development of convulsions. The patient is kept continuously partially narcotized and isolated in a dark room, with absolutely no disturbance. Whenever it is necessary to use the catheter, or to give an enema, a small quantity of chloroform is administered. This is also done before hypodermic injections are given. The chloral is usually combined with milk or broth, and the treatment is continued after the convulsions cease, the chloral being given in 20 grain doses, three times daily, often after the termination of pregnancy. So soon as the convulsions show a tendency to cease, labor is induced, and if the conditions are favorable the membranes are ruptured. Stroganoff reported 360 cases, with a mortality of 6.6 per cent. for the mother, and 21.6 per cent. for the child. In Roth's cases, in 23, convulsions appeared after the beginning of labor. These were immediately controlled by the treatment in 12 cases; after from one to three convulsions in 13; and after four or more in 6 cases. One mother died of empyema. Although the treatment could be carried out in the patient's home, it is better when done in a hospital, where complete control is more readily procured.

Twenty-five Cesarean Sections with no Fetal or Maternal Mortality.—Humpstone (*Amer. Jour. Obst.*, May, 1911) reports 25 cases of abdominal Cesarean section without fetal or maternal mortality. The indications were dystocia from ventral fixation in 5 cases, scar tissue in the vagina with funnel pelvis in 1 case, stenosis of the vagina in 1 case, impacted cyst in 1 case, contracted pelvis with prolapse of the cord in 3 cases, bony tumor of the pelvis in 1 case, generally contracted pelvis in 9 cases, funnel pelvis in 1 case, and flat rachitic pelvis in 3 cases. It is interesting to note that one-fifth of this series

were caused by previous ventrofixation; 3 of these cases followed operation by one man, who was accustomed to suture the fundus and posterior wall of the uterus firmly to the fascia, muscle, and the peritoneum just above the pubes. The other 2 cases were those of accidental fixation, where the operator intended to practise suspension. In 2 cases sterilization was accomplished by the removal of the tubes; and hysterectomy was done in 1 case because the vagina was so occluded that proper drainage could not be obtained. The operation was performed as rapidly as possible, and this was thought a valuable point in the technique. Two of the patients were operated upon a second time. A tendency to acute dilatation of the stomach was the most troublesome complication after operation, but was readily controlled by lavage. Three-fifths of the mothers nursed their children; the remainder were unable to do so. This series illustrates the extension of the operation in conditions other than contracted pelvis, and also the success of the operation when patients are taken in good condition.

Eclampsia and Anaphylactic Phenomena.—Fellander (*Zeitschrift f. Geburtshülfe und Gynäkologie*, 1911, Band lxviii, Heft 1) in a considerable number of experiments upon guinea-pigs found no reason to believe that eclampsia is an anaphylactic process. In his experiments he employed albuminoid material from the fetus, from the placenta, and from the amniotic liquid.

The Treatment of Children Apparently Stillborn.—Ahlfeld (*Zeitschrift f. Geburtshülfe und Gynäkologie*, 1911, Band lxviii, Heft 1) considers the old division of cases of apparent failure in respiration, into livid and pallid asphyxia, to be illogical and misleading. After trying various forms of treatment, he believes that when a child does not show signs of life promptly after delivery, the umbilical cord should be immediately tied and cut. The child should be placed in a warm bath and the surface of the body cleansed as quickly as possible, fresh warm water being added to the bath at a temperature of 38° to 40° C. An effort should be made to determine what the exact condition present is, and whether the respiratory passages are occluded. One must remember that the heart may not beat at short intervals, and the child still be revived; and again that a child may be practically dead although the heart continues to beat. After the circulation of the skin has been stimulated by the warm bath, and the air passages have been cleansed from mucus and meconium, the child is suspended by the feet, the chest is compressed gently, and an effort made to force out the mucus which may have been inspired. If respiration does not occur, the child is wrapped in a warm towel, a catheter passed into the trachea, and suction exercised to remove the mucus. If the heart is beating the child will usually make a deep inspiration and the heartbeat become stronger and more rapid. The physician can usually determine by the presence or absence of reflexes in the mouth and throat whether or not the child is actually living. Ahlfeld lays great stress upon gentle but persistent counterirritation of the skin in stimulating respiration. He would have the child rubbed with warm towels, or again placed in a warm bath and then thoroughly dried. Schultze's method of swinging the child should not be used

in premature and feeble children, or in children subjected to birth-pressure. He prefers to rely upon the warm bath, upon the use of the catheter in the trachea, and retains Schultze's method as a last resort. In his experience, if the child does not show signs of life after half an hour's treatment, its resuscitation cannot be expected.

The Production of Increased Resistance to Peritoneal Infection.—Hoehne (*Archiv f. Gynäkologie*, Band xciii, Heft 3, 1911) has made a series of experiments on 89 different animals to determine a method of increasing the resistance of the animal to peritoneal infection. In the case of rabbits, he found that intraperitoneal injections with moderate quantities of olive oil and oil of camphor in quantities as great as 10 c.c. were harmless; while quantities reaching from 20 to 100 c.c. threatened the animal by fat embolism in the lungs and produced local and general complications. These injections set up a reaction peritonitis, not peculiar to the oil employed, but a process which would be produced by any foreign body. This peritonitis increased the absorption of bacteria injected into the abdominal cavity. Rabbits so treated perish much sooner than those infected, but in whom the peritoneum had not been irritated. If, however, the reaction peritonitis had existed for at least twenty-four hours, the absorption of bacteria was very much diminished, and even entirely ceased for days or weeks. Animals so treated were able to resist bacteria which otherwise would have caused death. Poisonous bacteria injected after this preliminary peritonitis, were found to have perished in about four days after the injection. In animals not so treated, bacteria injected into the abdomen were absorbed in as short a time as three minutes.

Sixteen Unselected Cases of Hebostiotomy from the Clinics of Berlin, Munich, and Konigsburg.—Haarleicher (*Jour. of Obstet. and Gyn., of the British Empire*, March, 1911) reports 16 cases from the clinics mentioned. These cases are reported in detail, and the conclusions of the observer are of interest. The indication for hebostiotomy was indefinite. As a rule, there was a history of previous difficult labor, and the mother's urgent wish for a living child led to the performance of the operation. Primiparæ and cases with a true conjugate below $6\frac{1}{2}$ to 7 cm. and cases already infected, are considered unsuitable for the operation. The operation must be performed as a primary and elective one to be successful. Bumm's method consists in puncturing the tissues, while the needle is introduced under the guidance of two fingers in the vagina; while Döderlein makes an incision and introduces a blunt needle under the guidance of the finger between the soft parts and the bone. In the hands of skilful operators the operation is quickly and readily performed. The great advantage claimed that later deliveries would be easy because of the operation has not been demonstrated. The fibrous union which immediately follows the operation often gives place to an excessive deposit of callus which may prove a hindrance in a subsequent labor. In one case which first had bilateral hebostiotomy, Cesarean section was afterward performed. The cutaneous wound frequently suppurates and does not heal readily, and thrombosis is not unusual. Patients frequently suffer from throm-

bosis, prolapse, and sacral pain, and are unable to promptly return to their accustomed work. Although the technique of the operation, as now developed, is simple and exact, the morbidity is far greater than that of abdominal Cesarean section, in uninfected cases. To be successful, the operation must be very carefully chosen. It will have its best success in multiparæ with a true conjugate of not less than 8 cm. in a generally contracted pelvis, or 7.75 cm. in a simple flat pelvis.

An Improvement in the Technique of Cesarean Section.—Veit (*Zentralblatt f. Gynäkologie*, 1911, No. 16) has practised the following method of performing Cesarean section, and believes it to be an improvement. The incision is made in the linea alba, opening the abdomen at such a point that the umbilicus is in the middle of the incision. The abdominal wall is covered with aseptic material, and the uterus carefully delivered through the incision, with the patient in the Trendelenburg posture, the fundus lying upon the epigastrium. Moist sterile towels are then carefully packed behind the uterus and above it so that the abdominal cavity is completely shut off. The uterus is opened by a transverse incision, and the position of the patient makes the delivery of the child a very easy one. The after-birth is readily delivered. The contents of the uterus escape toward the chest of the patient and do not go into the abdomen, and the uterus is immediately closed by suture. The uterine surface is very thoroughly and carefully cleansed and the uterus replaced in the abdomen. Especial care is then taken to disinfect the abdominal walls and the abdominal wound is then closed. If the operator prefers to have the patient in the horizontal posture, the uterus is brought out to one side with the fundus over the patient's thigh. The point made by Veit consists in the care exercised to prevent the uterine contents from escaping into the abdominal cavity, and in his revival of the transverse incision across the fundus, which has been abandoned by many operators.

GYNECOLOGY

UNDER THE CHARGE OF

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Rupture and Perforation of Pyosalpinx.—Lejars (*Semaine Méd.*, 1911, xxxi, 169) reports the case of a woman, who, while in his ward awaiting operation for bilateral pyosalpinx, was suddenly seized with severe abdominal pains, accompanied by rigidity and tenderness, with elevation of the pulse and temperature. An immediate operation disclosed the presence of free pus in the pelvis, extending upward among the coils of small intestine. On the anterior surface of the right

tubal mass was a perforation the size of a lentil through which the pus was escaping. After supravaginal hysterectomy with drainage the patient made a satisfactory recovery. As a result of a study of this case, and others previously reported by him, as well as of the literature, Lejars comes to the conclusion that mechanical causes are not alone sufficient to account for a rupture of a pyosalpinx; that some alteration in the wall of an infectious or vascular nature must have been present, such as local ulcerations, creating a point of least resistance, small intraparietal abscesses, a softening, an edematous infiltration of the wall, a friability of the enveloping membrane, etc. Some such factor being present, however, then a mechanical agent may be the immediate cause of rupture. The latter may consist in the traction of adhesions, compression by surrounding organs, muscular effort, direct traumatism, normal labor, or the manipulations of an induced abortion. As to organisms causing the condition, the colon bacillus, gonococcus, and streptococcus have been described, and at least one case is reported of a pure typhoid bacillus infection of the tube with rupture occurring during the course of a case of typhoid fever and simulating intestinal perforation. At the operation a pure culture of typhoid bacilli was obtained from the pus. Lejars believes that in some of these cases the pus may be sterile, but that in the majority it is probably more or less virulent, as evidenced by the storminess of the symptoms and marked rise of temperature, which nearly always accompany a tubal rupture; also by the high mortality of these cases, this being 48.8 per cent. in a series of 45 cases reported by Bonney in 1909. Lejars lays stress, therefore, on the importance of early operation, the mortality in Bonney's cases operated on inside of twelve hours being but 30 per cent., whereas it rose to 80 per cent. after forty-eight hours. Another advantage of early operation is that usually the condition of the patient is such as to permit of a complete operation, and not merely drainage. The chief conditions with which a ruptured pysoalpinx is apt to be confounded are a ruptured appendix with a mass, and a ruptured tubal pregnancy.

Relation of Uterine Fibroids to Cardiac Insufficiency.—Payne (*Jour. Amer. Med. Assoc.*, 1911, lvi, 1324) reports 5 rather remarkable cases of marked cardiac insufficiency, presenting the typical symptoms of this condition, such as rapid, feeble pulse, dyspnea, etc. In 2 cases murmurs were present, and in 1 swelling of the ankles, associated with fibroid tumors of the uretus. In all of these cases the removal of the fibroids, which were not of excessive size, was followed by a complete disappearance of the cardiac symptoms; in 1 case, in which 14 gallons of ascitic fluid had been removed from the abdomen previous to operation, there was no return whatever of this condition up to one year after operation. As a result of the observation of these cases, and of a review of the literature on the subject, Payne comes to the conclusion that in many cases of uterine fibroids there are present symptoms of cardiovascular disturbances, the severity of which stands in no direct relation to the size of the growths, and that in some of these cases the symptoms are materially improved by the removal of the tumors. He believes, however, that in some cases of severe cardiac disturbance death may follow operation, and urges the importance

in all these cases of very rapid surgical technique, careful hemostasis, as little handling of viscera as possible, and the greatest care to avoid overtaxing the heart during the postoperative treatment.

Treatment of Purulent Peritonitis.—Krecke (*Monats. f. Geb. u. Gyn.*, 1911, xxxiii, 473) cites the experiments of Glimm on animals with the intraperitoneal injection of camphorated oil, after which a marked diminution in the resorption of bacteria could be demonstrated; this phenomenon being explained by Glimm on the theory that the oil filled the lymph channels, and thereby hindered absorption. He also cites the use of the same substance by Pfannenstiel and Höhne as a prophylactic before abdominal section in unclean cases, and by Hirschel in the treatment of 9 severe cases of generalized peritonitis, with 5 recoveries. Krecke states that on the strength of these experiences he has used it routinely in the treatment of such cases for some time, his material now amounting to 11 cases of diffuse, purulent peritonitis, all arising from perforated appendices. Some of these cases were light, others very severe; the ages of the patients ranged from eleven months to seventy years. In former years Krecke's mortality was from 34 to 42 per cent. in similar cases, but the 11 cases treated with camphorated oil all recovered. As there was no other change in the technique whatever, Krecke believes that this rather remarkable showing must be due to the effect of the oil. His method is to remove the appendix, sponge out the pus, and then pour into the abdominal cavity 100 grams of camphorated oil, which is swabbed about with a stalked sponge. The abdomen is then closed, one cigarette drain being introduced into the pelvis. The question as to whether the oil acts by mechanically plugging the lymph vessels, or by setting up a reactionary inflammation, is left undecided.

Results Obtained by the Radical Vaginal Operation for Carcinoma Uteri.—As a result of an experience covering ten years, Schauta (*Monatsschr. f. Geb. u. Gyn.*, 1911, xxxiii, 680), in an article which may be considered an answer to Wertheim's recently published monograph, gives in statistical form the results he has attained and his reasons for believing that in many cases the vaginal route is to be preferred to the abdominal for the removal of the carcinomatous uterus. During the period reviewed, 910 cases of carcinoma of the cervix presented themselves at Schauta's clinic; of these, 445 were operated upon, giving an average operability of 51.3 per cent. In 26 additional cases the operation was begun, but on account of technical difficulties, could not be completed. Of the 445 operated cases, 40 died, giving a primary mortality of 8.9 per cent. for the whole ten years; in the last three years, however, the primary mortality has been reduced to 3.7 per cent. In estimating the results with regard to lasting cures, only those cases are considered which were operated upon during the first five years; that is, those in which a period of at least five years has elapsed since operation. During this period, 447 patients presented themselves, 211 of whom were operated upon; of these, 73 remained cured after a lapse of five years, giving an "absolute percentage" of cures amounting to 16.6 per cent. of all cases that applied for treatment and to 39.7 per cent of all cases operated upon. In reckoning this absolute percentage,

Schauta counts all cases lost sight of, and all cases that died of intercurrent disease without autopsy among the recurrences, agreeing in this with Wertheim, and giving up all complicated formulæ. Judged in the same way, Wertheim's absolute percentage of cures is about 1.8 per cent. higher than Schauta's, but his operability is slightly lower (48.9 per cent.), and his primary mortality very markedly higher (18.6 per cent.), so that Schauta considers that, of two operations so nearly alike in endresults, the one with the lesser mortality is to be preferred in most cases as giving the patient a better chance for increased length of life. Schauta lays emphasis on the fact that his "radical operation" does not consist merely in making the Schuchardt paravaginal incision, this signifying here no more than the incision through the abdominal walls does in an abdominal operation. The important features of his operation are the careful preparation of the ureters, the ligation of the uterine arteries, the wide excision of the parametrium out to the pelvic walls, and the formation, as one of the first steps of the operation, of a vaginal cuff to prevent all contamination of the wound with matter escaping from the cervix. He shows that injury to the ureters occurred less frequently in his series than in Wertheim's cases, and that when it does occur it can be treated as satisfactorily (by means of suture, implantation, etc.) by the vaginal as by the abdominal route.

Pruritus Vulvæ.—Schubert (*Münch. med. Woch.*, 1911, lviii, 745) describes 2 cases of severe idiopathic pruritus vulvæ, in which all ordinary therapeutic measures had failed, which were cured by the injection into the sacral canal epidurally of 1.5 c.c. of a solution consisting of cocaine hydrochlorate, 0.1 c.c.; beta-eucaine, 0.1 c.c.; sodium chloride, 0.4 c.c.; distilled water, 200 c.c. In the first of these cases a like quantity of the same solution was injected into the region of the tuber ischii where the pudic nerve, which supplies the vulva and vestibule, comes to the surface. In both cases the cure was complete and apparently lasting. In 2 cases of severe sacral pain, in which no genital condition could be found to account for the symptoms, Schubert was able to attain a cure in 1 case and a marked improvement in the other by the same method. He reports, moreover, that in 25 other cases of pruritus or sacral pain treated in this way he has had most satisfactory results, especially in the pruritus cases. He believes that the factor of suggestion can be altogether excluded, as in almost all instances all possible therapeutic measures had been tried, but without avail, and is therefore convinced that the effect is due to a direct action on the roots of the pudic nerve.

Operation of "Utriculoplasty" for Uterine Hemorrhage.—Bonney (*Lancet*, 1911, clxxx, 1266) reports six cases of hemorrhage due to the condition commonly spoken of as "hemorrhagic" or "fibroid" metritis, in which, instead of doing a hysterectomy, he performed Kelly's operation of merely excising a wedge-shaped portion of the fundus uteri having its base upward and its apex near the internal os. In most of these cases sufficient mucous membrane was left on each side to maintain the communication between the uterine cavity and the tubes. Hemorrhage from the uterine walls was controlled by the sutures bringing them together. One of the cases was a woman, aged

twenty-nine years, who had been bleeding for months and was extremely anemic; she was entirely cured of the excessive hemorrhage, and subsequently became pregnant and went to term, being delivered of a healthy child. This pregnancy occurred within four months after the operation, that is, before the uterine scar could have become consolidated, and yet no ill effects followed. Bonney believes that the risk of this operation is certainly not greater than that of hysterectomy; that the uterine wall in these cases is not itself necessarily very abnormal, and that, therefore, it is not contraindicated to leave a portion of it behind; that the operation is a legitimate alternative to hysterectomy, and is certainly to be preferred in the case of young women anxious to have children.

DERMATOLOGY

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Starch Paste as a Vehicle in the Treatment of Scabies.—Yamada (*Dermat. Ztschr.*, 1910, xvii, Heft 4), in the treatment of scabies, employs a paste made of rice flour containing 30 per cent. of sulphur. This rice paste is prepared by mixing 40 to 45 grams of rice meal with ½ liter of water and, in order to prevent fermentation, 2.5 grams of salicylic acid or 5 grams of benzoic acid. This paste of rice and sulphur is employed in the same manner as the ointments commonly used, being rubbed in once a day for two to five days, the patient neither bathing nor changing his underwear during this time. The author has treated 44 cases in this manner, and has never seen relapses; and the duration of the treatment was in most cases shorter than with the usual methods.

Hot Air in Dermatological Therapeutics.—Ravaut (*Annales. d. dermat. et de. syphil.*, 1910, No. 3) reports the results which he has obtained in various affections of the skin treated by hot air. He employed the apparatus constructed by Gaiffe, in which air heated by an electric current to a temperature varying from 60° to 80° C. is projected through variously sized and shaped tips upon the skin. The hot air thus obtained is employed for various purposes: At a temperature not exceeding 80° an active hyperemia of the parts treated is produced; at an elevated temperature cauterization and carbonization of the tissues to a varying depth results. As complete immobility of the patient is necessary to obtain the best results, and as the pain is considerable, the author advises general anesthesia. Nevus, lupus, cutaneous tuberculosis, epithelioma, and leukoplakia are some of the more important affections in which this method of treatment was employed with more or

less success, the air being used at a high temperature for its cauterant effects. The hot air treatment was likewise employed to produce hyperemia in torpid ulcers; and cicatrization was more rapid in these cases than in those treated by the usual methods.

Bacteriology and Pathological Anatomy of Leprosy.—J. M. H. Macleod (*Brit. Jour. of Dermatology*, October, 1909) states that the researches of the last twelve years have only more firmly established the lepra-bacillus of Hansen as the specific cause of leprosy. During the last decade numerous attempts have been made to cultivate the bacillus, but no medium has been discovered on which it will invariably grow. It has not been proved that the bacillus is present and can lead a saprophytic existence on decayed organic matter, such as decomposed fish, meat, rice, or in the soil. This fact alone, the author thinks, is sufficient to negative the theory that the disease may result from the eating of decayed fish, decayed pork, and the like, and until the lepra bacillus has been found to exist in decomposed fish, "the fish theory of leprosy cannot be regarded as other than an hypothesis, which is unsupported by scientific fact." Numerous inoculation experiments made upon different animals have invariably given negative results. It would seem most probable that the lepra bacillus may gain entrance in various ways, the nasal and upper respiratory tracts being probably the most common, corroborated by the frequency with which nasal symptoms form one of the earliest manifestations of the disease. The bacilli are widely distributed throughout certain tissues of the body, but are absent from the muscles, bones, and joints. In the skin lepra bacilli have been confined as a rule to the corium, occasionally being found in the deeper layer of the epidermis, but it is doubtful if they exist in the sebaceous glands, as they have an aversion to fat. The bacilli may affect the nerves in their entire course, but observers are not of one mind as to the mode of invasion, especially whether the nerve involvement occurs first in the finer endings in the skin and ascends, or is a descending process, the result of a general infection.

Studies in the Metabolism of Certain Skin Diseases.—Johnston and Schwartz (*New York Med. Jour.*, March 13, 20, 27, 1910), in a series of elaborate studies undertaken for the purpose of demonstrating, if possible, by examination of the urine, some relation between disordered metabolism and certain inflammatory diseases of the skin, and for the purpose of discovering some means of preventing relapses in these diseases, conclude that none of the urinary compounds dealt with in these studies are likely to have any specific causal relation to the diseases considered. Since indicanuria, for example, occurs independently of lesions upon the skin and in all the forms of inflammation considered, this condition is not likely to have any direct causal relation to diseases of the skin. In view of the fact that disturbance in the nitrogen partition is most common in the prodromal period, and that it is associated with other symptoms indicative of intoxication, and that the figures return to the normal coincidently with improvement, the authors regard the conclusion justifiable that this change and the lesions upon the skin are the effects of a common cause which at the present time is not discoverable. These studies suggested nothing especially new in the

way of treatment. Regulation of the diet is regarded as of the first importance, especially as to the taking of proteids, which should be limited, or, in acute cases, even totally prohibited. Green fruit and vegetables are especially indicated. Medicinal treatment should consist of elimination by the bowels, kidneys, and skin. Saline cathartics with occasional doses of mercurials are better than antiseptics in intestinal putrefaction. Elimination by the kidney may be secured by the administration of large quantities of water alone, or saline diuretics may be used. The administration of thyroid or nucleoproteids of the thyroid, was found useful in prurigo and certain cases of dermatitis herpetiformis.

The Role of Staphylococci in Eczema.—Bruck and Hidaka (*Archiv f. Dermat. u. Syphilis*, 1910, x, Heft 1 to 3), in a series of investigations undertaken with the view of learning whether such biological changes in the blood serum of eczema patients could be demonstrated as would permit the conclusion that staphylococci had a share in the eczematous process, found that these organisms could give rise, in eczema, to biological reactions which were manifest as an increase in the agglutinin and antilysin content of the blood. They found, moreover, that the duration and severity of the eczema were not without influence upon the magnitude of this antibody production. Although it does not follow from the demonstration of these facts that the staphylococci or their toxins are the exciters of eczema, they believe that the view that these microorganisms play a harmless role in this disease must be given up.

Prurigo and the Papule with the Urticarial Basis.—O. H. Holder (*Jour. of Cutaneous Diseases*, April, 1911) considers this in its several aspects, calling attention to Richl's (of Vienna) views, who was the first to point out the true nature of the papule and that it was urticarial, and hence produced by a rapidly forming edema of the cutis, and that throughout the evolution of the papule its contents were and remained essentially fluid; owing to the absence of redness the term "pale papule" was applied to it. Dr. Holder goes into the subject of the pathology at some length, and concludes that he would endorse the views of those who believe that the papules are solely due to traumatism of the skin, and that they should be (as they now are at times) classified under the term papular urticaria.

The Surgical Treatment of Cutaneous Malignant Growths.—J. C. Bloodgood (*Jour. Amer. Med. Assoc.*, 1910, lv, 1615) bases his observations upon over 1000 cases, and of these, 65 were malignant pigmented moles, 45 sarcoma of the derma, and 812 epithelial tumors of the skin and mucous membranes. Of the malignant pigmented moles, not one was to be considered as a definitely cured case, but of 75 additional cases of benign disease there was no recurrence of internal metastasis. Incisions wide of the diseases are strongly advised. The epithelial tumors were classified according to their pathology into c. basocellulare, c. enbocellulare, and c. spinocellulare. The basic type is the least malignant of these; the squamous or spindle cell variety is the most malignant. Incomplete incision with the knife is more dangerous than failure to cure by other methods of treatment.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF
WARFIELD T. LONGCOPE, M.D.,
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Immunity in Tuberculosis. — Webb and Williams (*Jour. Med. Research*, 1911, xxiv, 1 to 4) have continued their investigations upon immunity produced by living tubercle bacilli. They report successful experiments made upon guinea-pigs which received, on the aggregate, more than one thousand times the lethal dose of living tubercle bacilli. A guinea-pig was inoculated weekly for 9 months with a tubercle culture of such virulence that 150 bacilli had been found sufficient to infect a guinea-pig. The inoculations were all made subcutaneously into the abdominal walls of the animal. On December 12, 1908, a guinea-pig received 2 live tubercle bacilli and weighed at this time 624 grams. Nine months later, September 16, 1909, the animal received 21,000 live tubercle bacilli and weighed 803 grams. The animal received in all 141,835 tubercle bacilli and remained perfectly healthy. Owing to an outbreak of guinea-pig cholera, it was necessary to discontinue the experiments. The animal was tested with tuberculin according to Römer's method. The skin fold before testing with tuberculin measured 4.064 millimeters. Twenty milligrams of old tuberculin were injected subcutaneously into the centre of this skin fold and twenty-four hours later there was a slight redness about the point of inoculation. The skin fold at this time measured 5.08 millimeters. The reaction was therefore considered negative. The animal was killed, and at autopsy all the organs, with the exception of the stomach and intestines, were found normal. The glands were not enlarged and there were no lesions at the site of the inoculations. Portions of lung, liver, spleen, and kidney, and one small inguinal gland were ground up in salt solution and injected into a guinea-pig. The injected animal remained healthy, thus indicating that in spite of the injection of this very great number of tubercle bacilli the animal remained healthy and was apparently immune. Webb and Williams conclude: "It may therefore be safely considered that a guinea-pig has received, without the production of tuberculosis, about 1000 times the lethal quantity of living virulent tubercle bacilli."

Anemia Produced by Bacterial Hemolysins.—Fejes (*Deut. Arch. f. klin. Med.*, 1911, cii, 129) has experimented with extracts of colon, dysentery, and typhoid bacilli to determine whether the injection of these substances is capable of producing anemia in animals. The cultures grown upon agar were suspended in salt solution and then extracted with alcohol at 37° C., these extracts were found to have a slight hemolytic power for dogs' blood *in vitro*. When injected into rabbits these extracts produced a distinct but moderate anemia. An attempt was then made to increase the hemolytic activity of these organisms by enhancing their virulence. For this purpose irritation of the gastro-intestinal tract was brought about in dogs and rabbits by means of chemicals, and later large quantities of cultures of the organisms were introduced into the stomach. Twenty-four to forty-

eight hours after the intestinal infection had been set up the animals were killed and the organisms recovered again from the intestinal tract. Extracts of the organisms which had caused these intestinal infections were found to have increased considerably in hemolytic activity *in vitro*. When the extracts were inoculated into dogs and rabbits a marked and rapid anemia developed, with reduction in both hemoglobin and red corpuscles. Polychromatophilia was observed and nucleated red blood cells, among which numerous megaloblasts made their appearance. Repeated injections proved fatal. In the rabbits there was a moderate leukocytosis; in dogs the total number of leukocytes was little changed, though the lymphocytes were both absolutely and relatively increased. The bacterial hemolysins caused, therefore, an anemia which, at least in dogs, was not unlike the pernicious type in man. These experiments lend support, therefore, to the view that severe anemia in man may be caused by the absorption of bacterial products from the gastro-intestinal tract.

Cirrhosis of the Liver.—Much confusion has always existed in the classification of the different types of cirrhosis of the liver, and it has been rather the terminal stages of cirrhosis that have been studied by the pathologists than the earlier lesions of this process. Mallory (*Johns Hopkins Hospital Bulletin*, 1911, xxii, 69), after a study of a large number of cases of cirrhosis of the liver, divides this lesion into five groups. The first group consists of the toxic cirrhosis, which includes the cirrhoses following central necrosis of the liver and is best exemplified by acute yellow atrophy. A study of these cases seems to show that when all the liver cells of a lobule were destroyed the bile ducts grow out a certain distance toward the hepatic vein, but they do not produce liver cells. Liver cells, on the other hand, originate only from liver cells and never from bile-duct epithelium. The production of fibroblasts (of new connective tissue) depends upon something more than the mere destruction of liver cells. The other four types of lesions terminating in cirrhosis show that fibroblasts multiply only when fibroblasts themselves have been injured or disturbed and thus lead to increase of the connective tissue. The second group consists of the infectious cirrhoses. This is comparatively a rare lesion. Infection travels along the portal spaces, causing an inflammatory reaction in this region, with formation of new connective tissue. In the third group, or the pigment cirrhoses, there is a direct lesion of the fibroblasts which comes with the deposition of pigment. Alcoholic cirrhosis which forms the fourth group is characterized by a peculiar hyaline degeneration of the cytoplasm of the liver cells preceding necrosis. In this same type the contraction of the connective tissue frequently compresses groups of liver cells so that they resemble bile ducts, but in these compressed liver cells it is often possible to demonstrate large fat vacuoles or hyaline material due to degeneration in the cytoplasm, neither of which occurs in the true bile-duct epithelium. In syphilitic infection of the liver which represents the last group the primary injury is due to the fibroblasts in consequence of which they often proliferate in excess. Contraction later of the collagen fibers produced by them results in compression and atrophy of the included liver cells. This direct injury to the fibroblasts by the Spirochæta pallida seems to be a general one and characterizes the specific action of this organism.

A Sarcoma of the Fowl Transmissible by an Agent Separable from the Tumor Cells.—Rous (*Jour. of Exper. Med.*, 1911, xiii, 397) for some time has been studying experimentally a sarcoma which occurred originally in a barred Plymouth Rock chicken and which has proved to be transmissible to pure bred fowls of the same species. The tumor, a typical sarcoma, composed of cells of a single type, only slightly differentiated and resembling young connective tissue cells, showed after passage through several generations an enormous proliferative power, growing rapidly at the site of inoculation, destroying the tissue of the chest and metastasizing by way of the bloodvessels to the lungs, heart, liver, and other viscera. When pieces of the neoplasm were transplanted into the breasts of chickens, the tumors arose from the transplanted cells, and a histological study of the tumor would not lead one to suspect that the growth could be transmitted by other means than a transplantation of the cells. It is well known, too, that cell-free extracts of the tumors of rats, mice, and dogs hitherto studied are innocuous and that inoculation of such extracts into animals does not give rise to tumors. It was found, however, that for this particular neoplasm the presence of tumor cells was not necessary in order to transmit the growth. At first the ground tumor suspended in Ringer's solution was filtered through paper, and the filtrate was discovered to be capable of producing a tumor identical with the original one when inoculated into Pylmouth Rock chickens. Next the tumor was ground up in Ringer's solution and centrifugalized at high speed. The supernatant fluid was again found to have the power of producing tumors when inoculated into chickens. Finally, the extract was passed through a Berkefeld filter impervious to Bacillus prodigiosus and the limpid filtrate when inoculated into chickens still gave rise to typical tumors. The neoplasm produced by these filtered extracts, moreover, could be transmitted from generation to generation by the same means. It thus becomes evident that the cause of the growth of this tumor in inoculated chickens is extrinsic to the cells of the infecting material. Rous suggests two theories to explain the action of the self-perpetuating agent in this sarcoma of fowls: (1) That it is a minute parasitic organism; (2) that there is some chemical stimulant elaborated by the neoplastic cells which might cause a tumor in another host and thus bring about in consequence a further production of the same stimulant. At the present time cultures from the growth in many media have remained sterile. Examinations of the filtrate and fresh smears from the tumor surface with the dark field illumination, and various histological procedures applied to the neoplastic tissues have failed to reveal anything which can be recognized as a parasitic organism.

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ORIGINAL ARTICLES

IS THERE SPECIFIC TREATMENT FOR DIABETES MELLITUS?[1]

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PRELIMINARY CONSIDERATIONS.

Vast as has become the accumulation of literature on diabetes mellitus, it is obvious that real advance in the knowldege of the disease demands still more facts. Though the observations to be detailed failed to sustain toward their conclusion the brilliant promise of therapeutic efficiency which rewarded the treatment of certain cases at the outset, it seems possible that the very failures may have value in the conception of an efficient working hypothesis.

Carbohydrates enter the stomach under a variety of complex chemical forms, but in the process of digestion and absorption they are transmuted chiefly to the relatively simple product, grape sugar or dextrose ($C_6H_{12}O_6$). When retained in the tissues, the soluble sugar appears to be reduced to a less soluble starch (glycogen), which is again converted into sugar preliminary to utilization. Sugar is said to occur normally in the human blood in a concentration of about 1 part to 1000. So essential to the metabolism of protoplasm is the carbohydrate molecule, that when this substance is not available, other foodstuffs, proteids and perhaps fats, undergo chemical transformations by which carbohydrate radicles are offered to the tissues. Whenever the proportion of sugar in the blood rises above 2 in 1000, the impermeability of the kidneys is

[1] Read before the Association of American Physicians, May 10, 1911.

overcome, dextrose passes through, and the result is glycosuria. Glycosuria is, as a rule, simply an expression of excessive concentration of sugar in the blood. The wonderful power possessed by the normal tissues of appropriating carbohydrate so as to prevent its accumulation in the circulation may be overcome experimentally by giving excessive amounts of sugar in the food. It is obvious that the physiological machinery which coördinates the metabolic activity of every living molecule with the varying supply of carbohydrate in the ration so as to provide working material for the cells while preventing an excess of sugar in the blood must be a mechanism of extraordinary complexity. *A priori*, it seems probable that lapses of efficiency in one or another part of this nutritive machinery should occasionally occur leading to a temporary glycosuria without implying any serious departure from the normal. It is also to be expected that the mechanism for carbohydrate metabolism should at times suffer from permanent defects in one or another of its parts, resulting in a more or less unmanageable tendency to the accumulation of sugar in the blood, thus giving rise to the pathological state known as diabetes mellitus. As the disorders leading to glycosuria demand for their explanation a knowledge of the normal carbohydrate metabolism of the body, diabetes is the one disease a discussion of which is attempted in every text-book on physiology. The *rationale* of the carbohydrate mechanism is made somewhat clearer by a consideration of the parallel system for the utilization of oxygen in the body. We know that the complex machinery of respiration subserves one prime double purpose, and is under the domination of one double force—the hunger of the tissues for oxygen and their intolerance of an excess of carbonic acid.

Adequate oxidation of the tissues and removal of carbonic acid presupposes the efficient coöperation of a great number of physiological events, such as the rhythmic discharge of the respiratory centre, normal elasticity of the lungs, and diffusion attributes of the air cells, sufficient contractile power of the heart and blood-vessels, and oxygen conveying power of the red corpuscles. These and many other functions regulate the procession of oxygen and carbonic acid through the body. When this process is acutely interfered with the physiological reaction is hyperpnea, in which group after group of muscles not ordinarily employed in respiration are set in action in the endeavor to satisfy the oxygen hunger of the tissues and abolish the irritation of the waste product. In an analogous way the whole metabolism of the body may be modified in diabetes in a desperate effort to give the tissues the sugar food they are denied. From a practical therapeutic standpoint our comparison is of further significance, for every physician knows that the efficient treatment of disturbances of tissue oxidation depends upon discovery of the specific erring function out of many which

may be at fault. In a similar way it is possible that the disease resulting in glycosuria may be indifferently produced by manifold different functional failures, and, as in the case of the respiratory dyscrasia, an efficient treatment can only be devised which shall correct the particular physiological function in fault. Such a conclusion brings bewildering complexity into the practical consideration of diabetes.

As the phenomena of respiration are essentially under the control of tissue metabolism, so it has become equally clear that carbohydrate in the body fulfils its function only in the molecules of the living tissue, and that the coördinate action of a considerable number of individual organs and their products is necessary to pilot the sugar absorbed through the complex route leading to its oxidation and excretion. When Claude Bernard, in 1849, produced glycosuria in a rabbit by his "piqure" experiment, puncture in a certain area of the floor of the fourth ventricle, it seemed as though the equilibrium of carbohydrate metabolism depended upon a balance between the nervous system and the liver protoplasm, for the glycosuria in question did not occur if the store of glycogen normally present in the liver was removed by starvation before the performance of the piqure. When Minkowski and von Mering, in 1889, showed that a severe and fatal form of diabetes followed the ablation of the pancreas from animals, it led to the demonstration that the pancreas furnishes to the body an internal secretion which is absolutely necessary to normal carbohydrate metabolism. Through Opie and others it has been rendered probable that this secretion is formed in the pancreas in the islands of Langerhans. The fact that extract of the adrenal body when injected into animals causes glycemia and glycosuria, and that extracts of adrenal body and pancreas mixed *in vitro* neutralize each other, led Zuelzer[2] to generalize the conclusion that the adrenal bodies and the pancreas play the part of physiological antagonists in carbohydrate metabolism, the former tending to mobilize the molecules into diffusible sugar and the latter to fix them in a more stable form in the tissues. Eppinger, Falta, and Rudinger[3] have carried on important researches upon the relations in carbohydrate metabolism of the internal secretions of the adrenals, the thyroid, the parathyroids (and chromaffin system), and the pancreas, in which it is made clear that mobilization or fixation of sugar depends more or less upon a balance between the activities of these glands. The pancreas and the thyroid, and the pancreas and the adrenals, intensely inhibit one another, while the thyroid and the adrenals are mutually stimulant in the production of glycemia. These authors made laborious determinations of the metabolism in dogs before and

[2] Deutsch. med. Woch., 1908, No. 32, S. 1380.

[3] Ueber die Wechselwirkungen der Drüsen mit innerer Sekretion, Zeitschr. f. klin. Med., 1908, 1909, etc.

after the extirpation of various glands of internal secretion. They found, for example, that in pancreas-free dogs at the height of metabolic disturbance the injection of adrenalin causes enormous increase of sugar and nitrogen elimination; whereas, like treatment in thyroid-free dogs caused no glycosuria. They hold that the glycosuria following piqure is due to a liberation of adrenal internal secretion. They conclude that while genuine diabetes has its origin in profound disturbances of equilibrium between the glandular organs regulating metabolism, the final cause of the disease remains in deepest obscurity.

Pflüger, the physiologist, in disputing the evidences for an internal secretion by the pancreas, found by experiments on frogs an important nervous connection between the duodenum and the pancreas.[4]

Severing these nerves leads to glycosuria. It is concluded that the duodenum is a peripheral regulating organ for sugar mobilization and an inhibitor of sugar formation.

Minkowski failed to confirm these results on mammals.

Pflüger holds that a nerve centre in the medulla controls the formation of diastase in the liver, and consequently regulates the rate of sugar production.

Cushing and others have shown that removal of the anterior lobe of the pituitary body is followed by metabolic disturbances in which glycosuria is one result.[5]

The ductless glands operate by internal secretions, which are absorbed by the circulation. The active agents in the secretions are known as "hormones," which "Starling defines as chemical messengers, which, formed in one organ, travel in the blood stream to other organs of the body and effect correlation between the activities of the organ of origin and the other organs on which they exert their specific effect. Such substances belong to the crystalloid rather than the colloid class; they therefore are thermostabile, and do not act as antigens when injected into the animal."

In an admirable review of the subject, Howell[6] points out that the hormone may act at least in two ways—either as a chemical stimulus, illustrated in the excitement of pancreatic secretion under the influence of secretin, or as an activator, in which role it simply develops some latent property of a chemical body, as by turning an inert proferment into an active ferment; according to Howell, "This at least would seem to be true for the hormone, of unknown nature, given off by the pancreas and concerned in the glycolysis of sugar in the organism."

However numerous may be the physiological defects which lead

[4] Quoted from Blumenthal, Deutsch. med. Woch., October 22, 1908.

[5] Johns Hopkins Hosp. Bull., May, 1910.

[6] The Chemical Regulation of the Processes of the Body by Means of Activators, Kinases, and Hormones, Science, 1910, xxxi, 93.

to glycosuria, we must believe that the fundamental nature of diabetes depends upon a disorder of tissue metabolism. As Halliburton puts it, "The difficulty in diabetes probably lies in an impairment of the capacity of the cells of the body to prepare the sugar for oxidation. In this process the sugar, or its early oxidation product, called glycuronic acid, is split into smaller molecules and ultimately leaves the body as carbonic acid and water."[7]

The current of modern observation, experiment, and speculation sets powerfully toward the conclusion that practically all the functions that we have been accustomed to define as the criteria of life in matter are carried on by protoplasm through the agency of quasi-adventitious radicles, which may join or separate from the protoplasm without altering its integrity. These radicles are known as ferments, or enzymes, for it is their fundamental peculiarity that they may cause a rearrangement of contiguous molecules without themselves being disorganized. They are essential agents in metabolism, whether of building up or breaking down. According to the view of Adami,[8] the enzyme radicle is not to be considered as a distinct molecular side chain of the cell, but rather that specific enzyme actions are a constitutional property of the living proteid molecule. There seem to be various orders of these intermediaries through which the reactions of living matter are invoked.

A conservative and accurate physiologist (Langley) maintains that the contraction of the skeletal muscle is not induced by the direct action of the motor nerve impulse, but indirectly through "receptive substances," which are interpolated between the nerve endings and the muscle, and which are not an integral part of the protoplasm, but are more or less intimately connected with it. Various drugs exert their effects by combining with the receptive substance. He believes that "nerve impulses can only cause contraction by acting on a receptive substance. . . . Curari, in combining with the receptive substances, simply prevents them (and so the contractile substance) from being influenced by nerve stimuli."[9]

It will, of course, occur to every one that the chief modern theory of immunity is founded on the assumption that a molecular intermediary, an adventitious side chain, correlates the reactions of tissue cell with the antigen.

That the muscle substance contains a glycolytic ferment has been established by a number of experimenters, and recently Ransom confirmed these results with the conclusion that, "It is possible to prepare from frozen muscle a plasma containing a ferment or ferments capable of converting glucose or glycogen into lactic acid, CO_2, and alcohol."[10]

[7] Diabetes Mellitus from the Physiological Standpoint, Practitioner, July, 1907, p. 1.
[8] Principles of Pathology, 2d Ed., i, 70 to 84.
[9] Jour. Physiol., 1909, xxxix, 236.
[10] A Contribution to the Study of Muscle Enzymes, Jour. Physiol., 1910, xl, 1.

The first important work in this direction was that of O. Cohnheim.[11] This author found that solutions of dextrose added to an extract of pancreas remained unchanged. A nearly equally negative result attended the mixture of dextrose with the expressed juice of muscle. But when muscle juice was added to the extract of pancreas, the mixture developed marked glycolytic powers, and considerable amounts of sugar added to it were destroyed. As this reaction occurred in a homogeneous, cell-free fluid, it must have been due to a ferment. The active substance of the pancreas withstood boiling and dissolved in alcohol, and therein resembles the active principles of the internal secretions of the adrenals and the thyroid rather than the class of ferments. It was found that the glycolytic power of the muscle-pancreas mixture was annulled by adding an excess of the pancreatic constituent. The maximum glycolytic effect was obtained when 75 grams of muscle was combined with about 0.8 gram of pancreas. Cohnheim's experiments have been repeated by a number of experimenters, some of whom have confirmed and others failed to obtain his results. To this latter group belongs Simpson,[12] a late worker on the subject.

Still more recently P. A. Levene and G. M. Meyer have submitted the problem to renewed investigation, and seem to have resolved much of its obscurity. They found, like Cohnheim, that a solution of glucose lost much of its reducing power when digested with a muscle-pancreas mixture. Nevertheless, this result does not indicate, as had been assumed, loss of sugar by oxidation, but rather a concentration of the carbohydrate molecules into osazones, which do not respond to the cupric reduction test.[13]

Building on these ideas, Zuelzer attacked the clinical problem of diabetic therapeusis.[14] He discovered that in animals made glycosuric by the exhibition of adrenalin the urine became sugar-free after the intravenous injection of an extract of pancreas. He concluded that there exists a physiological antagonism between the adrenal and the pancreatic hormones, and that diabetes was the result of the balance of power turning in favor of the former. By a method whose details are not disclosed, he made extracts from the pancreatic glands obtained from living animals at the height of digestion. In several severe cases of human diabetes, he made intravenous injections of this pancreatic extract, with the result of causing the sugar to disappear from the urine for three or four days. The patients usually suffered from a severe chill following the treatment.

W. M. Croftan describes a severe case of juvenile diabetes in which

[11] Hoppe-Seyler's Zeitschr. f. Physiol. Chemie, 1903, S. 336; 1904, S. 401; 1906, S. 253.

[12] Biochem. Jour., 1910, v. 126.

[13] On the Combined Action of Muscle Plasma and Pancreas Extract on Glucose and Maltose, Jour. Biolog. Chem., April, 1911, p. 96.

[14] Zeitschr. f. Exp. Path. u. Therapie, 1908-09, Band v, S. 307.

favorable results followed the administration by mouth of dried pancreas in capsules, followed by capsules of secretin.[15] Later, he reports success in the administration of a commercial extract of pancreas.[16]

At an earlier date A. C. Croftan[17] found great diminution of sugar excretion in diabetic patients to whom he administered a mixture of expressed muscle juice and pancreatic extract. As no further results are reported, we must conclude that later trials were unsuccessful.

ORIGINAL WORK.

My own interest in the study of diabetes mellitus was but general in character until a little patient, a girl, aged seven years, under my care, was found to have a glycosuria which, at first manifested only in the morning urine and amenable to regulation of the diet, later became constant and unmanageable. In despair, a mode of treatment was adopted which was formulated on theoretical considerations. For a time the results were so definite and happy that I was encouraged to pursue the general plan of treatment in other cases. The therapeutic outcome in certain subjects has been of such a character as to warrant a record of the observations. These studies have been greatly extended through the cordial coöperation of certain professional colleagues, in particular Dr. Moses Kleiner and Dr. S. Ringolsky, who enjoy an exceptional clinical experience with diabetes mellitus.

At this place, also, may be expressed my deep obligations to Professor J. C. Todd, of the University of Colorado, for many scores of estimations of urea and ammonia in the urines of my patients. Cordial thanks for advice or assistance is also due to Professor W. D. Engle, of the University of Denver; Dr. P. L. Leyda, of the County Hospital, and to Dr. R. T. Woodyatt, of Rush Medical College.

THE THERAPEUTIC EFFECTS OF MUSCLE INFUSIONS IN DIABETES MELLITUS.

In reflecting on the physiological errors involved in the establishment of diabetes, it seemed to me probable that one vital link in the pathology consisted in the lack or insufficiency of some tissue side chain, receptive body, or enzyme, by means of which the healthy tissue cells are alone enabled to appropriate the sugar in the blood. One naturally turned to the skeletal muscles as offering the principal storehouse of this glycogenic (or glycolytic) tissue

[15] Lancet, February 27, 1909, p. 607.
[16] Dublin Jour. Med. Sci., May, 1910, p. 332.
[17] New York Med. Jour., 1904, lxxix, 882.

enzyme. While it might be suspected that such an atomic group would be destroyed if operated on by the digestive apparatus, it is pertinent to recall the statement of Anderson,[18] that sensitization of an animal to a strange proteid is produced by feeding with it.

Method of Preparing the Beef Juice. One pound of lean beef is ground in a sausage machine and then covered in a jar with a pint of cold water, to which thirty drops of "dilute" hydrochloric acid are added. At times, one quart of water and one dram of acid are used. The mixture stands in the ice box all night, or at room temperature for four hours, and is then strained through cheesecloth. The liquid should be drunk in the course of the day, one-half to one tumblerful at a time. The meat residue should remain nearly dry and colorless.[19]

An excellent device for expressing the juice is made by folding a strong towel once and stitching the ends round two strong sticks. The fabric should be cut so that an oblong bag is made about 11 inches wide by 6 inches deep. The moist beef is placed in this, and the sticks twisted to make pressure.

Case I (patient of Dr. M. Kleiner, who furnished the following notes).—J. P., male, aged seventy-two years; weight, 190 pounds. Lived in Socorro, N. M. Had suffered from glycosuria for about twenty years. A sister had also suffered from diabetes. He developed diabetic cataract in both eyes during 1908. He was examined by Dr. Kleiner first in December 1909. The patient was then passing 80 to 120 ounces of urine, containing 4 to 6 per cent. of sugar. He was kept on a strict diet until May, 1910, with but slight influence on the sugar excretion. Dr. D. H. Coover refused to operate for cataract, on account of the serious condition of the patient. Dr. Kleiner placed the patient on the acid-beef infusion described above, and in two days all traces of sugar had disappeared from the urine. Dr. Coover removed the cataract from the right eye on May 2, 1910. There was slow healing, without pain or iritis. On May 30, with appropriate glasses, vision in the right eye was normal. The strict diet was discontinued, but the beef juice was partaken of for twenty days after the operation, the glycosuria remaining in abeyance and the general condition of the patient improving in every way. The patient returned to his home in New Mexico, and passed from definite observation. Messages were received at intervals conveying news of his continued well-being until February, 1911, when a relapse was announced. A specimen of urine received at this time had a specific gravity of 1021, and contained a small amount of acetone and about 2 per cent. of sugar.

[18] Anaphylaxis, Johns Hopkins Hosp. Bull., July, 1910, p. 221.

[19] My friend Dr. G. B. Webb has reminded me that this is essentially the beef soup long ago advised by Dr. S. Weir Mitchell in his classic Fat and Blood in the treatment of neurasthenic cases. I have frequently employed it with satisfaction in disorders marked by malnutrition, especially tuberculosis.

Case II (patient of Dr. M. Kleiner).—J. H. H., female, aged fifty-eight years, fairly well nourished. The patient was reckless of any rules of diet. She had had symptoms of diabetes for more than seven years. The urine contained from 3 to 6 per cent. of sugar, 50 to 90 grams in twenty-four hours, and a large amount of acetone. She was frequently prostrated with spells of great muscular weakness. During such an attack the administration of beef infusion was begun early in April, 1910. Within about three days after beginning this treatment the patient recovered her normal strength and energy, which remained with her while the treatment was continued, about two months. The glycosuria and acidosis were unrelieved by the treatment, and in June an attempt was made to improve the patient's metabolism by the administration of pancreatic extract, as in Case VII, but without success. As might have been expected, revulsion against the unpalatable mixtures caused rejection of the whole plan of treatment. The patient went from bad to worse, and died in April, 1911, in diabetic coma, complicated with uremia.

Case III (patient of Dr. M. Kleiner).—N. H. C., female, aged forty-seven years. On a strict diet, her urine contained 5 per cent. of sugar, and she was losing weight. Beef infusion has been given, at first to the amount of 1 quart; later, 1 pint daily. Now, after three weeks, the patient is gaining weight, she feels much better, and the sugar excretion is reduced to 0.5 per cent., with a diet to which are added daily three slices of toast and a small baked potato.

Case IV (patient of Dr. M. Kleiner.)—J., female, aged sixty-seven years. A bad case, characterized by emaciation, neuritis, and dyspnea. The urine contained a high percentage of sugar, besides albumin and casts. She has taken beef infusion on alternate days for eight weeks. There is improvement as to the pain. The urine is free from sugar, although rice with a teaspoonful of sugar daily is added to the diet.

Dr. Charles G. Duncan, of Socorro, N. M., the family physician of Case I, writes under date of March 31, 1911: "I have used the beef juice in two cases (of diabetes), and have found excellent results. One was a merchant (aged sixty-nine years), in whose urine I found large quantities of sugar. He took the beef juice . . . for two days, then waited two days before commencing again. This was kept up for two weeks, when I could not find a trace of sugar. The other case was a lawyer (aged forty-three years), who had some sugar in his urine, and the results with him were equally as good."

Discussion. It is, of course, unnecessary to dwell upon the well-known fact that the clinical course of diabetes mellitus is at times apparently subject to amelioration under a great variety of

conditions and remedies which probably have no specific relation to the pathological process. It is clear that a much more profound study of the cases which have been presented would be necessary in order to establish the real meaning of the apparent therapeutic effect of the raw-beef infusion. It should be noted that at least the first four cases presented were refractory to ordinary rules of treatment. If further observation should support the hypothesis which led to the treatment—namely, that by such means the body could be furnished with a muscle enzyme capable of metabolizing sugar—an encouraging advance will have been made in the knowledge of diabetes.

Particular attention is called to the age of the half-dozen patients in the foregoing list. All were beyond middle life. Reference will be made later to other subjects, mostly younger in years, in whom little or no success attended the treatment.[20]

THE USE OF MUSCLE INFUSIONS COMBINED WITH OR FOLLOWED BY WATERY EXTRACTS OF PANCREAS.

Pursuing the same line of argument which holds deficiency of a muscle enzyme responsible for certain cases of diabetes, is but applying current notions of physiology to assume that such an enzyme needs, like the complement of blood plasma, an amboceptor to direct its energies, or, like trypsinogen in the duodenum, an activator such as enterokinase to develop its ferment qualities. We naturally look to the internal secretion of the pancreas to furnish this intermediary body, which may, indeed, play a role quite different to those which have been indicated. In the last few years many attempts have been made to correct the diabetic dyscrasia by the administration of extracts of pancreas, and certain of the results have been very encouraging.

The present article deals with a single instructive case in which for a time there was evidence that extracts of muscle and pancreas played a coördinate action in abolishing glycosuria. That the therapeutic desideratum finally failed itself demands an explanation which is well worth seeking.

Case VII.—A. S., a girl, aged seven years. Her birth had been premature a month or more. Each year she had suffered an attack of bronchitis in the fall and spring, expecially severe when eighteen months old. The child was abnormally bright until the age of four

[20] After this paper was in type my attention was led to the brilliant lectures delivered by T. Lauder Brunton nearly forty years ago (Pathology and Treatment of Diabetes Mellitus, Brit. Med. Jour., 1874, i, 221). The author not only dwelt upon Schultzen's conception of a glycolytic ferment in the body, but deduced the conclusion that the course of diabetes might be favorably affected by feeding patients with raw beef, so as to supply deficiency in glycolytic muscle enzyme. The therapeutic application was meager and the result disappointing.

and one-half years. She was then greatly frightened, incidental to an operation for the removal of her adenoids, and for more than two years thereafter her mental brightness was less conspicuous. Glycosuria was first detected in March, 1908; she had been more or less invalided with colds all winter. The sugar at first was found only in the specimen of urine passed on rising in the morning. This was true whether the principal meal of the day was taken in the evening or at midday. For some months the glycosuria was controlled by a fairly strict diet containing no sugar and a minimum of starch. In December, 1909, she was prostrated with an infection causing enlargement of the cervical glands and serous inflammation of the middle ears. Thereafter sugar reappeared in the urine, and persisted, at least in the morning specimen, in spite of the strictest diet.

Definite observations were initiated upon the child about this time, in which I had the invaluable assistance of an intelligent mother, with her heart in the work. A rather marked icteroid hue or bronzing of the skin was apt to distinguish periods of glycosuria. The mother frequently remarked that exhibition of the beef infusion (as described below) was immediately followed by an obvious improvement in the child's spirits and brightness, and by a diminution in her abnormal appetite.

The observations in this case included a continuous record of the quantity and specific gravity of the urine secreted, with an estimate by the fermentation test of the sugar eliminated in each twenty-four hours. For a prolonged period, Professor Todd made daily estimations of the amount of urea and ammonia contained in the urine. A mere trace of acetone was constantly present in the urine, the amount apparently varying proportionately with the glycosuria. Only on one day, during an intercurrent attack of bronchitis, was it considerable.

The term "strict diet" embraced such articles as bacon, eggs, butter, cream, cabbage, tomatoes, cauliflower, lettuce, and spinach. When the patient's tolerance for carbohydrates was surpassed through the addition of toasted bread to the strict diet, the carbohydrate was withdrawn as soon as the projected experiment was concluded. Periods of a week or two were allowed to elapse between observations made to test the carbohydrate tolerance of the patient. It is worth noting that the break in carbohydrate tolerance on a given diet was marked first by the appearance of a minute quantity of sugar in the urine, but the amount rapidly increased. For obvious reasons, the observations were cut short in each case without attempting to work out the progress of this glycosuria. That the welfare of the patient did not suffer during this course of experiments is certified by the fact that whereas at the beginning her tolerance for carbohydrates was *nil*, toward the close of the series more than three ounces of bread per diem could be consumed

with impunity. For the sake of brevity, the clinical course of the case will be described merely in outline.

The patient having suffered with persistent glycosuria on a strict diet, on March 20, 1910, was begun, and continued for three weeks, the daily administration of a beef infusion, prepared essentially as described. Under this treatment the twenty-four hours' urine was occasionally free from sugar, but this at once reappeared on the addition of an ounce of bread to the diet. It may be said that with a beef infusion without acid, or in one in which the hydrochloric acid was replaced by an equivalent amount of acetic acid, the results seemed less favorable. On April 15 the daily output of sugar having ranged from *nil* to $\frac{7}{8}$ per cent., one ounce of wheat bread (toasted) was added to the ration. The glucose excretion rose to 9 to 14 grams per diem. On the 19th the acid-beef infusion was resumed, and given daily. The sugar excretion increased to 15 grams on April 22. The simple beef infusion was now abandoned, and in its place was given a mixed beef-pancreas infusion. This was made by soaking about six ounces of ground, fresh beef pancreas in one quart of water acidulated with 1 dram of dilute hydrochloric acid. After standing all night in the ice chest the mixture was strained, and to the fluid was added one pound of ground beef. After remaining four hours at room temperature the mixture was again strained and the juice was consumed by the patient in the course of twenty-four hours. The sugar excretion during the day on which the "mixed" infusion was administered reached 14.67 grams ($1\frac{5}{16}$ per cent. of the urine). On the following day, the diet remaining the same and no infusion being given, the sugar excretion fell to less than 7.6 grams, which could easily have been a fortuitous fluctuation. At the beginning of the second day, after exhibition of the mixed infusion, there was begun the administration of a pancreatic infusion. This was made by extracting about one-half pound of ground, fresh beef pancreas with one pint of water acidulated with 30 drops of dilute hydrochloric acid. From the time when the administration of the infusion of pancreas was begun the excretion of sugar ceased. The daily ounce of bread was now removed from the ration, and the urine remained sugar-free without treatment. At the same time there was improvement in the patient's general condition.

It was now important to determine whether the sugar had been driven from the urine by the pancreatic infusion alone or through some relation *in vivo* between the pancreatic infusion and the infusions which had preceded it. Accordingly, on April 28 there was added to the strict diet two ounces of bread. This caused the excretion of about $7\frac{1}{2}$ grams of glucose in the corresponding twenty-four hours. On the following day, under the same diet, a pancreatic infusion was given as before. The amount of sugar excreted rose to more than 16 grams. It was then concluded that an infusion

neither of beef, beef-pancreas, nor pancreas when given alone was capable of abolishing glycosuria, but that they might be effective when given in sequence.

The last member in this sequence was the pancreatic infusion; it was to be determined whether the efficient first member was the simple beef infusion or the mixed beef-pancreas infusion, which, according to Cohnheim, should give rise to a specific compound *in vitro*. The urine of the patient on a strict died having been sugar-free for some days, on May 15 and for three days following there were added 2 ounces of bread to the ration. Glucose to the amount of nearly 7 grams appeared the first day and rapidly increased to over 16 grams, so that on May 19 the amount of bread was reduced to 1 ounce per diem; nevertheless, the quantity of sugar still increased to over 18 grams. The administration of beef juice on the afternoon of the 19th and morning of the 20th was without effect on the glycosuria. But on the afternoon of the 20th there was given an infusion of pancreas, made by extracting 2 ounces of fresh pancreas with 1 pint of water, and the urine became sugar-free for the following twenty-four hours. Though strict diet was now resumed, a trace of sugar reappeared in the urine for three days; the diminished tolerance probably depended on a lowered resistance involved in an attack of bronchitis, for which the patient was confined to bed, and which, like frequent similar attacks, was possibly an expression of the general metabolic dyscrasia.

Without further treatment, for a period of three weeks following, with the exception of one day, the urine remained completely sugar-free, although the addition of bread to the diet was resumed and the daily amount was increased to as much as 3 ounces, which was the limit of tolerance. It appeared from the last series of observations that an established glycosuria could be abolished by a sequence of beef infusion followed by pancreatic infusion, and that, moreover, the effect of treatment was to greatly increase the range of tolerance for carbohydrates.

It was evidently of great practical moment in the therapeutic régime that an efficient substitute should be found for the fresh pancreas, which is difficult to obtain and most unpalatable. Two preparations were used with this end in view—namely, a proprietary pancreatic powder known as "Holadin," and a glycerin extract of fresh pancreas. The results were disappointing. It appeared that a glycosuria might be held in check but not abolished by administration of beef infusion followed in some hours by a series of Holadin capsules, representing 10 to 20 grains of the powder. It may be repeated that the general state of well-being of the patient appeared at its best not on the "strict diet," but when the largest amount of carbohydrate within the limit of tolerance was added thereto.

Renewed tests (June 18 and 25) were now made to verify the

favorable results previously obtained by the administration of a sequence of beef and pancreatic infusions. To my chagrin the treatment was without effect. Tolerance for carbohydrates, which had been overcome by 2 to 3 ounces of bread in the ration, was by no means increased by the treatment. Reflecting on these discordant results, it was surmised that a combination of the beef and pancreas extracts, such as had been used in the first successful experiments, might be necessary in the treatment of glycosuria. This notion was tested early in July. The addition of 3 ounces of bread to the ration caused the appearance of more than 9 grams of glucose in the urine during the same day in which a mixed infusion of beef and pancreas was given. The following day, under the same diet, with the addition of a pancreatic infusion (made by extracting for three hours 3 ounces of fresh pancreas with one pint of water acidulated with 30 drops of dilute hydrochloric acid), the urine became at once sugar-free. Here for the second time a sequence of mixed beef-pancreas infusion followed by pancreatic infusion had abolished the glycosuria.

Continuing the diet containing 3 ounces of bread per diem, sugar again appeared in the urine, but evidently the patient's tolerance had greatly increased, for whereas formerly carbohydrate tolerance had been overcome by much less than 3 ounces of bread, and when once broken the glycosuria had rapidly increased, now 3 to 4 ounces of bread caused the excretion of less than 3 grams of sugar per diem.

The child now (July 15) was placed for a time on strict diet, and the infusion treatment was repeated in preparation for a vacation in the country, where she went in a few days, in excellent condition, enjoying an ounce of bread daily with impunity. While in the country for some two months the diet had included 9 ounces of oatmeal (moist) and 2 gluten wafers daily; but the mother, who had learned to make the Fehling test for sugar, found after a time that the slightest indiscretion in diet was attended with glycosuria.

Very gradually the limits of tolerance became restricted, and in December, 1910, a small amount of sugar appeared even on a strict diet. Treatment with infusions of beef and pancreas was no longer effective. The glycosuria gradually increased, and now in April, 1911, the urine contains not only 30 to 40 grams of glucose per diem, but gives a rather strong reaction for acetone, and for the first time contains a trace of albumin.

Much might be said in the way of discussion on this case, but the results would necessarily be barren for lack of essential data. There was no obvious relation between the amounts of urea and ammonia excreted and the condition as to glycosuria.

There can be no reasonable doubt that the occasional abolishment of glycosuria was a genuine effect of the treatment. It is, of course, open to suspicion that the frequent administration of the beef infusion led to the formation of an antienzyme, yet it is hard

to reconcile such an explanation with the physiology of carnivorous animals. An extract of liver was partaken by the patient on one occasion, and work along this line seems desirable.

The report on a half-dozen other cases of diabetes treated according to the method described may be put in a few words, since the results were practically negative throughout.

Case VIII (patient of Dr. S. Ringolsky).—M., female, aged forty-one years. Had manifested occasional glycosuria since the age of twenty years. Any nervous excitement or overstrain increased the condition. The pleasant relaxation of a vacation would greatly increase her tolerance for carbohydrates. Sugar appeared in the urine when 4 to 5 ounces of bread were added to the diet, and the quantity was not decreased for the few days while the treatment was pursued.

Case IX (patient of Dr. Ringolsky).—W., female, aged about forty-eight years. Sister of the above. On a general diet she had excreted upward of 70 grams of glucose per diem, with a small amount of albumin. Her carbohydrates were limited to 3 ounces of bread; her glycosuria under treatment varied between 40 and 50 grams.

Case X (patient of Dr. Pothuisje).—Wb., female, aged fifty-nine years. On a strict diet she excreted 40 to 80 grams of sugar daily; only a slight amount of acetone. The results of treatment were negative.

Case XI.—R., male, aged about thirty years. Miner by occupation. The man was reckless in his habits; diet could not be certified to, though he was confined to bed in the county hospital. When first seen he passed urine to the quantity of about 350 fluidounces per diem, containing nearly 890 grams of sugar. Nevertheless, he claimed to feel strong and well. There was marked reaction for acetone, and Professor Engle found a maximum of 7 grains of oxybutyric acid in the first few days. Though the amount of urine and quantity of sugar excreted underwent a great diminution under treatment, the latter could not be regarded as successful. In this and the following case a profuse diarrhea was sometimes present. This was probably occasioned by the infusions. On one occasion, following diarrhea, the quantity of urine fell to 38 ounces, but the proportion of sugar rose to over 15 per cent. The man developed thromboses and general dropsy, and he died about two months after abandonment of the observations.

Case XII.—M. F., male, laborer, aged about forty-two years. Inmate of the county hospital. Not confined to bed. On a general diet he was passing 324 ounces of urine, containing nearly 912 grams of sugar, in twenty-four hours. He was treated with infusions of beef and and of "Holadin." The sugar excretion did not fall much below 300 grams per diem. Diarrhea was frequent during the observations. The patient claimed to feel much better for the treatment, but he was discharged as unimproved.

Conclusions. 1. Evidence has been presented that in a certain proportion of diabetics beyond middle age the metabolism and general symptoms may be improved and the sugar removed from the urine, at least temporarily, through the administration of an infusion of lean meat acidulated with hydrochloric acid.

2. In a single case of youthful diabetes (Case VII), though neither beef infusion nor pancreatic infusion was alone efficacious, when the one followed the other, or a mixture of the two after an interval of some hours, the urine became sugar-free. After the disease had persisted for some months this happy result could no longer be obtained. Nevertheless, the treatment, especially with the beef infusion, seemed to improve the subjective condition of the patient.

3. No good results attended the use of the commercial pancreatic powder employed.

PASSING LEAKAGE OF THE PULMONARY VALVE.*

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Incompetence of the pulmonary valve due to organic disease is a very rare condition. Only 24 cases were noted at Guy's Hospital out of 16,000 postmortem examinations during a period of thirty-two years,[1] and 3 among 24,000 cases admitted to the medical wards of Johns Hopkins Hospital.[2] But leakage may occur much more commonly here when the flaps of the valve are normal, but the ring to which they are attached is so dilated that the normal flaps are no longer able to close the enlarged orifice. It is with this latter condition, the so-called relative incompetence, that we are here concerned.

Relative incompetence is a condition not easy to demonstrate post mortem, and many cases, no doubt, occur during life, and have been carefully described, in which the valve was found at the autopsy to be competent. R. B. Preble[3] and others have published cases in which post mortem the pulmonary valve was incompetent and would not hold water, and yet the flaps were normal in every way; but it is easy to understand that, as long as any elasticity remains in the structures about the pulmonary orifice, this ring will tend to return to its normal size as soon as the pressure stretching it is removed. Thus, a valve which has leaked freely during life may post mortem appear to be normal, and may even hold water,

* Read by title before the Association of American Physicians, May 10, 1911.

which, after all, is at almost no pressure. In the writer's opinion such temporary leakages are far from uncommon, and he notes with pleasure a recent statement of Dr. Thayer to the same effect.[4]

Relative incompetence must be due either to (*a*) an increased blood pressure within the pulmonary artery and right ventricle, or to (*b*) a want of resistance to stretching of the tissues about the orifice. The question of exactly what tissues may be here involved need not be gone into, but Hugh Stewart two years ago demonstrated before the Association of American Physician the importance of the muscular ring below the aortic orifice in preserving the integrity of that orifice, and, according to G. A. Gibson,[5] Arthur Keith has shown that a loss of tone in the muscular fibers surrounding the mouth of the pulmonary vessel allows of stretching of the fibrous tissues.

Most cases of relative incompetence of the pulmonary valve that have been described have occurred as a sequel to mitral disease, especially mitral stenosis (Graham Steel) and fibrous disease of the lungs. It has been shown by Foxwell, Stacey Wilson, and others how easily the pulmonary artery dilates under internal pressure as compared to the aorta—six times as easily, after making all allowance for the different strains under which they work—and a number of workers have further endeavored to find the amount of pressure required to dilate the pulmonary orifice so as to produce leakage there.

G. A. Gibson found that a pressure of $14\frac{1}{2}$ inches of water was sufficient to cause a strong jet of water to escape through the pulmonary orifice in a sheep's heart; and in the same way a healthy human heart leaked freely at a pressure of 13 inches of water, and slightly with the pressure down to 8 inches.

We have tried a number of hearts in the same way, and on the whole with about the same results.

A bullock's pulmonary valve leaked freely at a water pressure of $6\frac{1}{2}$ feet, but long before this pressure was attained the pulmonary artery was ballooned in a marked fashion. When a string was loosely put round the orifice before the pressure was raised, no leakage occurred up to nine feet.

Seven human hearts were similarly tested, and they leaked freely under pressures varying from 11 to 18 inches, and often below that amount to a slight degree.

When the pressure is gradually raised in the pulmonary artery, the vessel very easily dilates in a balloon-like manner, the sinuses of Valsalva standing out with special prominence. Then after a certain pressure is reached a jet of water escapes from a small opening which appears at the apices of the flaps of the valve. If, however, one encircles the orifice with the fingers or with a previously adjusted ligature, the pressure may be raised to several feet without any incompetence of the valve occurring. This would suggest that

the leakage is due to dilatation of the ring around the valve, and not to any distortion due to the dilating of the pulmonary artery. Under Professor Brodie's suggestion the latter experiments were done without any previous alteration of the relations of the pulmonary artery to the aorta or heart, and finally with the heart still *in situ* in the cadaver and with the pericardium unopened. These precautions did not make any appreciable difference in the results.

In none of the experiments could the aorta be made to dilate to any extent, even under a pressure of 20 feet of water, much less could the aortic valve be made to leak. There was one exception to this in the case of a heart from a boy, aged two years, who had died of whooping cough, with complicating pneumonia. Here the aorta leaked at 8 feet, and before the leakage occurred the aorta did not dilate much. The endocardium about the orifice was greatly congested, as was also the mitral valve.

As the pulmonary artery dilates so easily even under a moderate pressure (and in these experiments it is shown that after the dilatation reaches a certain point the orifice shares in it so that leakage occurs), one would expect that such dilatation and even leakage would commonly occur during life, always with the proviso that the tissues dilate during life with anything like the pressure that they do in the cadaver. The mean blood pressure in the pulmonary artery is 17.6 mm. of mercury in the cat, 12.07 mm. in the rabbit, 29.6 mm. in the dog, according to Bentner,[6] and Gibson says that "pressure in the pulmonary artery in man at the height of a vigorous systole of the right ventricle may be well above that which first causes an insufficiency." No one believes that the normal pressure ever makes a normal pulmonary valve leak, but if the pressure be raised or the tissues be relaxed, then dilatation of the artery may and can often be demonstrated to have occurred; and if the orifice shares in this stretching, leakage may be produced even to a sufficient extent to cause a murmur, such a yielding of the orifice being no doubt largely due, as Stewart and Keith have urged, to a want of tone in the muscular ring just below the orifice.

The following three cases are ones in which an evident mitral lesion so raised the pulmonary artery blood pressure that that vessel and along with it the pulmonary orifice dilated and a murmur occurred, which came and went in two of them over a period of years.

Case I.—V. A., girl, aged thirteen years. Admitted to the Victoria Hospital for Sick Children last August, suffering from pericarditis and double mitral disease, with a marked accentuation of the pulmonary second sound.

October 18 the following note was made: Pulmonary second sound still much accentuated, and is now accompanied by a distinct short murmur. This murmur is localized to an area about the size of a penny over the pulmonary area and a little below it. It is unaffected by holding the breath.

October 26. Whole precordium heaves with each pulsation of the heart. On auscultation a double mitral murmur is heard; also a pulmonary diastolic.

November 6. Mitral murmurs only present. Pulmonary second much accentuated.

November 24. Diffuse heaving pulsation of the whole precordium. In the second left interspace two pulsations are seen, of which the outer is the earlier. (The outer is probably the left auricle and the inner the dilated pulmonary artery.) Double mitral murmur present, but no diastolic murmur, with the pulmonary second. This sound is much accentuated.

Case II.—A. P., girl, aged fifteen years. When seen on February 19, 1908, she was suffering from fever and pains in various joints. Within a few days the heart became markedly irregular and a mitral systolic murmur developed. This murmur became gradually more marked, and was present in all postures of the body. The pulmonary second was accentuated.

Two months later chorea developed. The mitral murmur was still present, and had become almost musical in character.

In June (two months later) it was noted that chorea was still evident, and the patient has developed flat foot. Mitral murmur still present, and the pulmonary second sound is markedly accentuated. A slight diastolic murmur is audible down the sternum. It is not heard in the neck. The heart is still irregular, giving an occasional quick beat. Apex is in the fifth intercostal space, just outside of the nipple line. No thrills. When patient sits up the second sound at the base becomes double and the diastolic murmur is more evident.

July 19. White blood cells, 5000. Heart again somewhat irregular. Diastolic murmur about the third left costal cartilage very evident.

October 16. Mitral systolic well marked. Pulmonary second sound much accentuated, and no murmur accompanies it in any posture. Cardiac deep dulness reaches from one-half inch beyond right of sternum to the nipple line. Apex in nipple line in the fifth space.

April 15, 1909. Feels well, and choreic movements are practically gone. Mitral systolic well marked, as is also the pulmonary second sound, which, however, is pure.

July 20, 1910. Seems quite well, but heart rather wide upon percussion, and mitral systolic murmur evident, and the pulmonary second sound is plus and accompanied by a distinct murmur. The pulse is not water-hammer in type, nor is there any bounding of the vessels in the neck.

Case III.—Female, aged thirty years. Came on April 4, 1904, complaining of cough and shortness of breath, which had been frequent during the last few years. The note then made was that

some bronchitis is found. Cardiac apex in the fifth space in nipple line. Here, first sound is flapping and a slight presystolic murmur is audible. A diastolic bruit is heard over lower part of sternum, but no capillary or water-hammer pulse present, nor are the vessels in neck bounding.

February 19, 1905. Presystolic murmur not heard, but a slight diastolic one audible, best marked over lower part of sternum. First sound sharp at apex.

November 19, 1906. Has had one of her frequent attacks of bronchitis. Careful examination of the heart reveals a marked presystolic murmur at the apex, with a flapping first sound. Absolutely no other murmur is audible, and the second sound is pure everywhere.

February 19, 1907. Bronchitis again. Diastolic murmur again, audible about the lower part of the sternum. Apex is in nipple line, in fifth space. No murmur heard in the neck, and here the second sound is well heard and is free from impurity.

May 15. First sound flapping at apex. Second sound is pure everywhere.

These three cases are all examples of the so-called Graham Steell murmur, in that there was present well-marked mitral disease, which presumably so raised the blood pressure in the pulmonary artery as to cause from time to time leakage at the pulmonary valve. In the following cases, however, no such cause seemed to exist, and probably the leakage was more due to relaxed tissues about the pulmonary orifice than to any marked increase in the blood pressure of the pulmonary artery.

Case IV.—Mrs. C., aged thirty years. Was first seen in March, 1904, for a slight attack of appendicitis. It was then noted that she had an aortic diastolic, with well-marked second sound. Pulse was regular and not of the water-hammer type.

Two years later, in November, 1906, aortic diastolic murmur not heard. Heart sounds are all quite clear and pure.

April 5, 1907. Aortic diastolic murmur now quite evident.

Dr. Finlay, of Montreal, had previously had this patient under his care, and on my writing to him about her, he replied as follows: "I remember Mrs. C.'s case quite well. She had a soft diastolic murmur, localized about the pulmonary area, but without the compensatory enlargement or the vascular phenomena of aortic incompetence. I always felt a little uncertain as to the significance of the physical signs. I can recall another case of a diastolic aortic murmur in which at several subsequent examinations it was inaudible."

March 17. The diastolic murmur is quite evident. The heart does not appear to be enlarged.

November 13, 1910. The pulse is regular and not water-hammer in type. No throbbing in the neck. Cardiac apex is in fifth space

one inch outside of the nipple line. The sounds are clear at the apex, but down the left border of the sternum there is a slight diastolic murmur. The pulmonary second sound is accenutated. There is no murmur in the neck. The liver is of normal size.

In this case, as the notes show, both Dr. Finlay and myself presumed that the murmur was of aortic origin, but I now believe that it was an example of occasional leakage at the pulmonary orifice.

Case V.—G. W. H., aged fifty-five years; farmer. Seen last November, with Dr. Brown, of Elmwood. Suffered from pernicious anemia of at least two years' duration. His chief complaints were of weakness and dyspnea. This note was made: Pulse regular and not of water-hammer type. Cardiac apex in fifth intercostal space half an inch outside of nipple line. No epigastric or venous pulse. Right border of cardiac dulness does not reach beyond sternum. At the apex there is a slight systolic murmur, and the second sound is clear. In the aortic area the sounds are both clear, and the second is not accentuated. In the pulmonary area the second sound is much accentuated, and is accompanied by a well-marked diastolic murmur. This is best heard about the inner part of the second left intercostal space, but can be heard for about an inch below this point. It persists through all phases of respiration, but is loudest at the end of expiration, and when the breath is then held. A well-marked pulmonary systolic murmur is also present.

Of course, in this case some old organic lesion of the pulmonary valve may have been present, but this is unlikely both on account of the rarity of such and also from the fact that until two years before the patient had been in rugged health.

Diagnosis. The chief classical sign of pulmonary regurgitation is a diastolic murmur best heard on the left side of the sternum, chiefly at the end of expiration, and not audible in the vessels of the neck nor at the cardiac apex. Along with this murmur there are signs of enlargement of the right heart with displacement of the apex toward the left. There is an absence of the water-hammer pulse and of a capillary pulse. The pulmonary second sound may be weak or absent, all depending upon whether or not the diseased flaps are able to close.

In the cases, however, where the leakage is due not to organic disease, but to relative insufficiency of the valve, the first thing usually noted is the accentuation of the pulmonary second sound, which loud sound is from time to time accompanied by a murmur of the above distribution. In all the cases so far noted by the writer the murmur has not been constant, but no doubt it often is persistent, especially when due to some permanent obstructive condition farther on in the pulmonary circulation, such as mitral stenosis or pulmonary fibrosis.

Prognosis. The importance of relative insufficiency of the pulmonary valve, of course, depends upon the fundamental cause of

the leakage. Where this is mitral stenosis—probably the most common permanent antecedent of the condition—it points to a considerable obstruction at that orifice, but even then the cases may do well for years, as in Cases II and III of our series, and after several years of known pulmonary leakage seem little the worse.

Where the leakage is due rather to a relaxed condition of the tissues about the pulmonary orifice the prognosis depends entirely upon the cause of this relaxed state. Dr. Thayer[4] mentions the condition as occurring in exophthalmic goitre, and as this disease lessens, one would expect the pulmonary leakage to stop.

A pulmonary systolic murmur, the commonest of all functional bruits, probably depends upon a dilatation of the pulmonary artery, and in most cases tends to disappear. When, however, the dilatation involves the pulmonary orifice so that a diastolic leakage occurs the condition is of more import, although even yet it may completely clear up.

From the dilatable character of the pulmonary orifice, and on the other hand the resistant nature of the aortic one, it seems probable that most of the diastolic murmurs which come and go—and which are usually reported to be aortic in origin—are due to passing leakage at the pulmonary valve.

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FURTHER CLINICAL STUDIES IN THE AUSCULTATORY METHOD OF DETERMINING BLOOD PRESSURE.[1]

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In a previous paper[2] we described in full the auscultatory method of determining blood pressure, giving details of technique, with explanation of sounds heard, and calling attention to the importance

[1] Read before the College of Physicians, May 3, 1911.
[2] Univ. Penna. Med. Bulletin, November, 1910.

of making accurate and repeated sequence readings. It may be repeated, briefly, that the method was described by Korotkow in 1906, and consists in constricting the brachial artery above the elbow in the usual manner, and then listening over the vessel at the bend of the arm. As the pressure is released a remarkable cycle will present itself. First will be heard a loud, clear-cut, snapping tone, the first phase, which is followed by a second phase, consisting of a succession of murmurs. The third phase begins with the disappearance of the murmurs and the appearance of a tone resembling in a certain degree that of the first phase, but less well marked, which soon becomes less clear in quality, or dull. At this point the fourth phase begins, and is followed by the disappearance of all sounds, the fifth phase.

In our first paper we emphasized especially the value of noting (1) tonal arrhythmias in distinguishing between functional and well compensated cardiac diseases; (2) the absence of the fifth phase in aortic insufficiency; (3) the determining of the percentage of phase length to pulse pressure, instead of measuring in millimeters only. We suggested that more attention should be devoted to the study of the relation of individual phases one to the other, instead of laying stress on one phase alone, as other observers have done. Our clinical data was insufficient on which to base accurate conclusions concerning this point, and our object was to devote a second paper to this subject.

During the past year's study we have not found it necessary to alter the conclusions reached in our first paper, so this part may be dismissed with no further discussion. Instead, we have devoted special attention to sequence reading and to their interpretation, and it is to this aspect alone that the present paper is dedicated.

A normal cycle of auscultatory phenomena consists of five phases, the systolic pressure being 130 mm. and the diastolic 85 mm. mercury. The phases are clear-cut, and bear a definite relation to the differences between the extremes of pressure.

The phases in millimeters average as follows: First phase, 14 mm.; second phase, 20 mm.; third phase, 5 mm.; fourth phase, 6 mm. Expressing it in terms of percentage based on the pulse pressure, we find since the pulse pressure equals 45 mm. that the phases have the following percentages: First, 31.1 per cent.; second, 44.4 per cent.; third, 11.1 per cent.; fourth, 13.3 per cent., or a total of 99.9 per cent.

We interpret variations in sequence readings by assuming that each phase has a physiological factor in its production in addition to the anatomical unit, and though our hypotheses have not the firm basis of an experimental control, yet clinical experience has lent some weight to their probable correctness. Our views in this regard may be set forth as follows:

1. The first phase, or tone phase, serves principally as an index as to how far the pressure must fall before the blood current can be sustained past the obstruction in the vessel caused by the cuff, at a sufficient velocity and for a sufficient duration to produce the murmur. Hence the information it affords is of negative rather than of positive value. In other words, its normal duration is of no value, but an increase or decrease in length is of importance.

2. The second, or the murmur phase, seems to be especially dependent upon cardiac effectiveness, for it is in this phase alone that the individual sounds possess a distinct element of duration, and this protracted energy, for so it must be regarded, must evidently come from the heart.

3. The third phase, or second tone phase, depends not alone on cardiac efficiency, but also on the character of the vessel wall. The more sclerotic the vessel and the greater the cardiac hypertrophy, the more favorable are the conditions for the production of a clear tone.

4. As the fourth phase, or dull tone, may be produced by a resilient vessel receiving a normal pulse shock, or by a rigid vessel receiving a weakened shock, its interpretation is more difficult, but its study quite as interesting.

If our assumptions as stated above are correct, then it is quite evident that increases in the second and third phases are dependent on cardiac strength and circulatory efficiency, while the first and the fourth phases suffer increase when there is cardiac weakness. Furthermore, in dealing with increases or decreases in any particular phase, it is important to know at the expense of what adjacent phase this has occurred. It is apparent that an increase in the third phase, for example, at the expense of the second, has not the same significance as an increase of this phase at the expense of the fourth. In the first instance the unit of cardiac strength, which we obtain by adding the lengths of the second and third phases, has not been materially changed, while in the latter it has been increased. For this reason, we recommend that the sum of the second and third phases be compared with the sum of the first and fourth phases, in order to determine whether the elements of force or those of weakness are predominating.

We reiterate the statement made in our previous paper, that, aside from the value of the persistence of the fourth phase in aortic insufficiency, little of diagnostic value has developed in regard to the length of any individual phase. Advantage has been derived, however, from studying the changes in the sequence readings, especially in decompensating cardiac lesions, as the patient improves or not. In these cases changes in the percentages of the various phases are not the only significant feature, but internal peculiarities appear. Or, to put it another way, sequence readings have a functional rather than an organic significance.

Our results uniformly show that with decompensation, or circulatory disturbances of lesser degree, the element of heart weakness (the sum of the first and fourth phases) progressively encroaches upon that of heart strength (the sum of the second and third phases). The second phase appears to be the one which is with most difficulty sustained, and often the internal variations, to be spoken of later, within the element of heart strength, precede the shortening of this element as a whole. The fourth phase, as weakness gains the ascendency, is usually the first to lengthen the element of cardiac weakness by its encroachment on the third phase, but encroachment of the first phase on the second soon adds its share to the total.

We have said that not only is the relation of the element of heart strength to that of heart weakness altered, but internal changes early appear. By internal changes we mean changes occurring in the phase itself, not as regards length, but pertaining to the relation of each individual sound to the other. Tonal arrhythmia is the most prominent of these, and simply means that there is to the ear, alternation in the intensity of individual sounds—arrhythmia of tone. We regard this form of arrhythmia as an evidence of variation in the force of individual cardiac contractions, and makes us aware of any departure from the normal before it can be discovered by palpation of the pulse or by auscultation of the heart. Tonal arrhythmias most frequently make their appearance toward the upper end of the sequence. They are first noted either as a failure of the first phase to be instituted after the first tone reaches the ear, or by a poor differentiation between the first and second phases in which tone and murmurs may alternate for a few heart beats. Internal variations in the third phase appear as the condition of cardiac weakness progresses, and are shown by alternating dull and sharp tones or by tones of different intensity. In cases when the arrhythmia is easily apparent to the ordinary method of examination, disturbance of auscultatory phenomena in the sequences is so pronounced as to be apparent even to a casual observer.

As a case of decompensation improves, the element of heart weakness gives place to the element of cardiac strength. The tonal arrhythmia and lack of differentiation between phases gradually disappear, commencing in the region of the third and fourth phases, and finally disappearing in the upper half of the sequence reading.

Our studies in the differentiation of cardiac neuroses from organic cardiac affections have not been met with results proportionate to the above detailed findings in other conditions, principally from a lack of material. We have had, however, a few striking cases which lead us to advance more strongly our belief that marked disparity in consecutive sequence readings, lack of uniformity in consecutive systolic and diastolic pressure estimations, when associated with internal variations in the various phases as shown by tonal arrhyth-

mia and poor differentiation, point strongly to the presence of a cardiac neurosis when a decompensatory cardiac lesion can be excluded.

We have chosen to illustrate the above by reporting briefly our findings in two cases:

CARDIAC NEUROSES.

Case I.—O. R., male, aged twenty years, dental student. Chief complaint, nervousness, palpitation, dyspnea, and precordial oppression, with general weakness. On examination the heat was apparently normal — no murmurs, no arrhythmia, and cardiac dulness normal. We reproduce two readings taken within a few minutes of each other.

I.		II.	
145		135	
	35.7 per cent., first phase.		44.4 per cent., first phase.
120		115	
	14.3 " second phase.		44.4 " second phase.
110		95	
	50.0 " third and fourth phases.		12.2 " third phase.
75		90	
Pulse pressure, 70.		Pulse pressure, 45.	

Tonal arrhythmia was marked throughout the entire sequence. Note also variations in successive systolic and diastolic pressures, and complete change in character of sequences.

Case II.—Eliz. M., aged twenty-eight years, housewife. Chief complaint, cardiac palpitation, dyspnea, indigestion, headache, and nervousness. On examination there were no signs of cardiac weakness, no murmurs, and no arrhythmia. Successive readings on the same day:

I.		II.	
130		117	
	28.3 per cent.		27 per cent.
115		107	
	28.3 "		54 "
100		87	
	24.5 "		5 "
87		85	
	18.9 "		14 "
77		80	
Pulse pressure, 53.		Pulse pressure, 37.	

Tonal arrhythmias were present, but were not so marked as in Case I. Here again are to be noted marked variations in systolic, diastolic, and in pulse pressure, also in character of sequences.

ANEMIA.

We have found the phases in anemias to be very loud and clear, and although the patient is extremely weak and relaxed, the

sequence readings assume an appearance of strength. This we ascribe to the anemic condition of the blood rather than to any intrinsic cardiac efficiency.

Case I.—Martin B., aged thirty-eight years. Diagnosis, progressive pernicious anemia. Chief complaint, weakness and shortness of breath on exertion.

118

22 per cent., first phase.
31 " second phase.
33 " third phase.
14 " fourth phase.

60

Pulse pressure, 58.

Blood: Hemoglobin, 30 per cent.; red blood corpuscles, 1,690,000; leukocytes, 3000.

Case II.—Margaret S., aged forty years. Diagnosis, progressive pernicious anemia. Chief complaint, edema, dyspnea, palpitation.

128

18 per cent., first and second phases.
74 " third phase.
8 " fourth phase.

43

Pulse pressure, 85.

There are marked tonal arrhythmias at the upper end of the sequence, the tones and murmurs alternating in such a way as to make accurate phase measurements impossible. The third and fourth phases were well differentiated and free from arrhythmias, despite edema, dyspnea, and palpitation

Blood: Hemoglobin, 18 per cent.; red blood corpuscles, 780,000; leukocytes, 6600.

POLYCYTHEMIA.

Since in anemia the phases are loud and clear and well marked, by analogy it might be anticipated that in polycythemia the opposite should obtain. Heretofore there has been no such case studied, but through the kindness of Dr. Klaer we have had the opportunity of making blood-pressure estimations in such a condition.

William B., aged about forty-two years. Diagnosis, polycythemia.

I.		II.	
128	December 23, 1910. No phases obtainable. All sounds distant and muffled.	114	January 3, 1911. No phases obtainable. All sounds weak and muffled.
105		93	
	Pulse pressure, 23.		Pulse pressure, 21.

Blood: Hemoglobin, 100 to 110 per cent.; red blood corpuscles, 8,000,000 to 11,000,000.

Our surmise was correct, for there was no differentiation of the phases possible, and the sounds had a "sticky" quality which defies description. This is the first case of polycythemia reported in literature studied with the auscultatory method of determining blood pressure, and exhibits the features which some German observers contended would accompany such a condition.

We have been interested in charting in a graphic form the blood-pressure results obtained in various conditions. These charts are based on the percentage length of individual phases to the pulse pressure. The first one represents a normal sequence in a young subject with a healthy heart and soft arteries, and shows graphically the ratio of cardiac strength to cardiac weakness, 55.5 to 44.4. We abbreviate as follows: Cardiac strength (C. S.); cardiac weakness (C. W.).

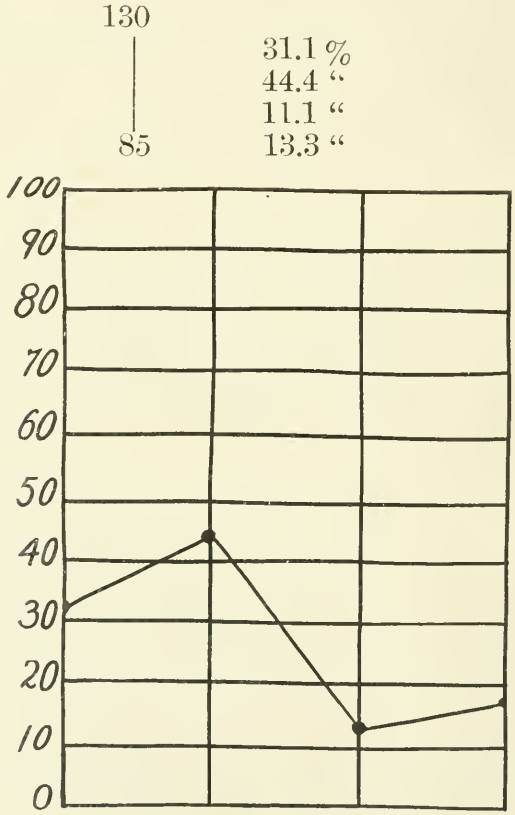

CHART I.—Normal sequence.

Considering next the pathological conditions and attempting to chart them in like form, we encountered some very interesting things.

MITRAL STENOSIS.

On admission the patient was slightly dyspneic, with duskiness of lips and hands. The chart shows graphically the elements of cardiac strength to be below those of cardiac weakness. C. S. : C. W. = 42 : 58.

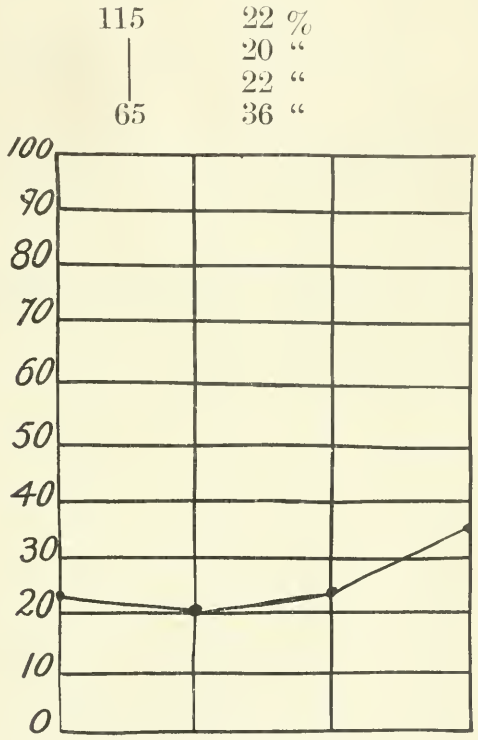

CHART II.—Mitral stenosis.

The next week on treatment there was a distinct change in the blood pressure readings. Here in the appended Chart III is well shown the increase in the lengths of the second and third phases, with a corresponding decrease in the first and fourth. The ratio of cardiac strength to cardiac weakness is 72.5 to 27.6, and the patient was subjectively and objectively improved.

MITRAL REGURGITATION.

CASE I.—The patient, a man, aged forty-nine years, came to the dispensary complaining of cough, palpitation of heart, and dyspnea on slightest exertion. There was dilatation of the right and left ventricle, with extrasystoles and marked arrhythmia. Tricuspid insufficiency, with pulsating liver.

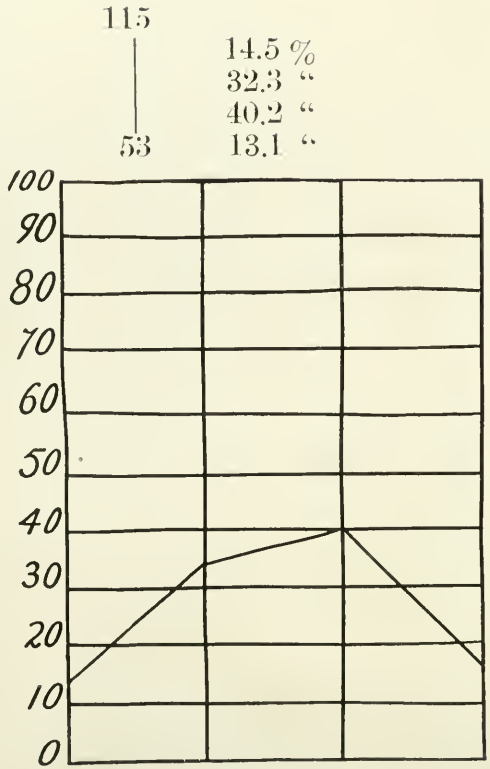

CHART III.—Mitral stenosis.

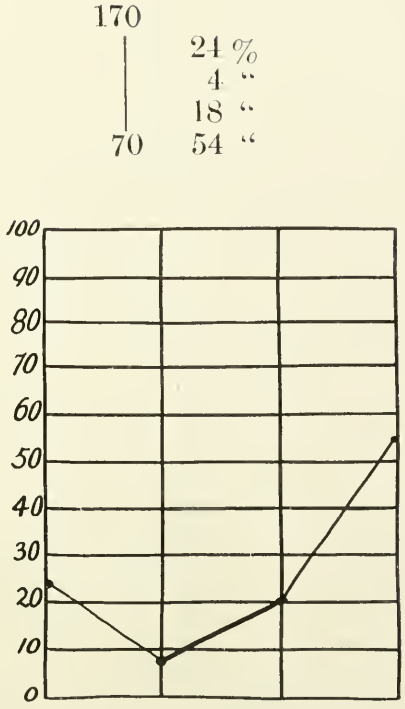

CHART IV.—Mitral regurgitation.

There were time and tonal arrhythmias, and this factor was obtained: C. S. : C. W. = 22 : 78 (Chart IV). Later readings with improvement of the patient developed the following curve:

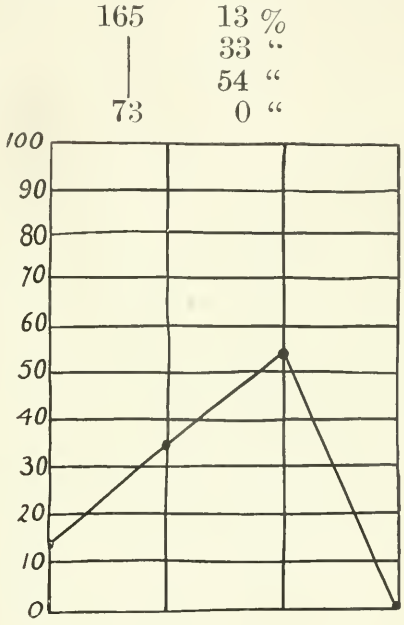

Chart V.—Mitral regurgitation.

There were no tonal arrhythmias, and C. S. : C. W. = 87 : 13. No fourth phase was obtainable.

Case II.—On admission the patient, a man, aged eighty-three years, had failing compensation secondary to mitral insufficiency, with dilatation of right and left heart. Marked arteriosclerosis.

On admission C. S. was below C. W., there was marked tonal arrhythmia, and the phases could not be differentiated. Subjective and objective improvement were noted, and with this the two curves became divergent, the C. S. remaining above C. W.

The sequence reading is herewith appended, and bears a striking resemblance to the foregoing case, when his heart became compensated. The increase in the length of the third phase is explained by arteriosclerosis in both cases, but in Case II the arteriosclerosis was very marked.

The appended chart represents the curve of the cardiac condition under treatment. The continuous lines represent the cardiac strength and the dotted lines the weakness.

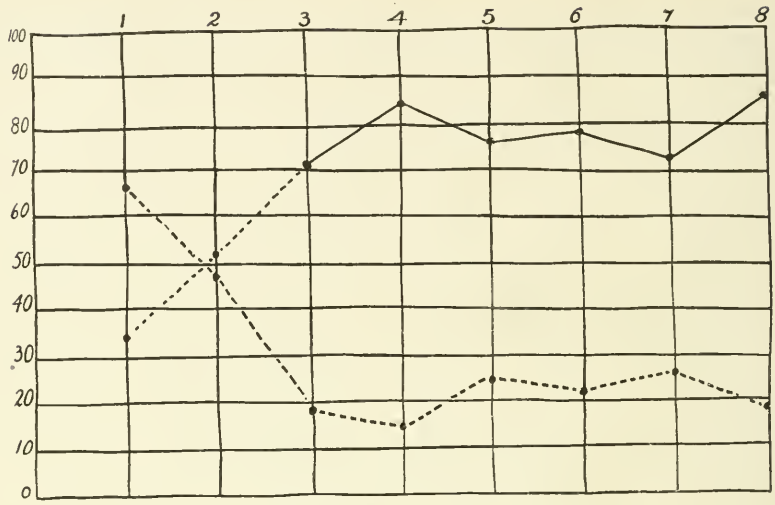

CHART VI.—Mitral regurgitation.

AORTIC INSUFFICIENCY.

On admission the blood-pressure reading was:

188
|
0

15 %
3 " C. S. : C. W. = 59 : 41
56 "
26 "

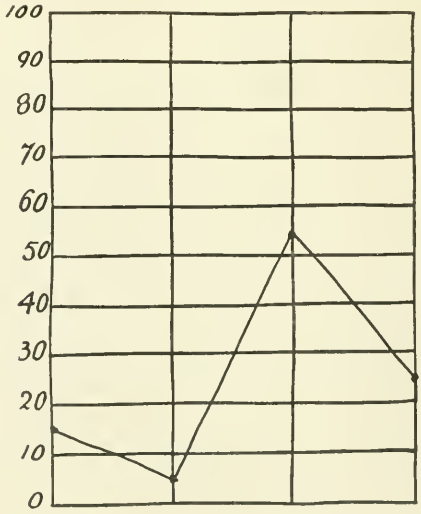

CHART VII.—Aortic regurgitation. On admission compensation poor.

The pathognomonic sign of aortic insufficiency—namely, absence of fifth phase—was seen.

On account of high blood pressure, we wished to try the effect of nitrites on the circulation, with what result is graphically seen in the following chart:

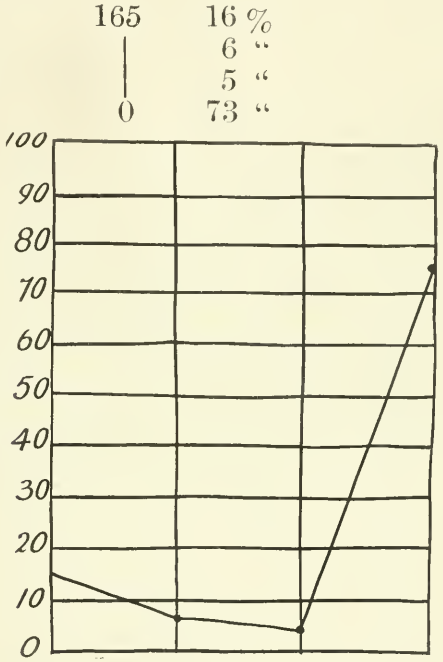

CHART VIII.—Aortic regurgitation. Effects of nitrites prior to recuperation of heart muscle.

The blood pressure was reduced, but withal there was a falling off of C. S., so that the ratio now was C. S. : C. W. = 11 : 89.

The medication was immediately discontinued, and with fair compensation there was a return of the ascendency of C. S. over C. W.

On this day blood pressure showed the figures represented in Chart IX.

The course of the disease is well shown by Chart X, in which we have depicted the cardiac strength (solid line) and the cardiac weakness (dotted line).

1. On admission (Chart VII).
2. Effect of nitrite (Chart VIII).
3. Condition of circulation improved.
4. Improvement more marked (Chart IX shows this sequence), and the patient, contrary to our advice, returned to work (ten hours on his feet as motorman).

5. As a result of the work the patient's condition became much worse, and he had to quit. The man was ill with dyspnea and marked edema, and was advised to enter the hospital. Refusing to do this, he left the dispensary and never returned.

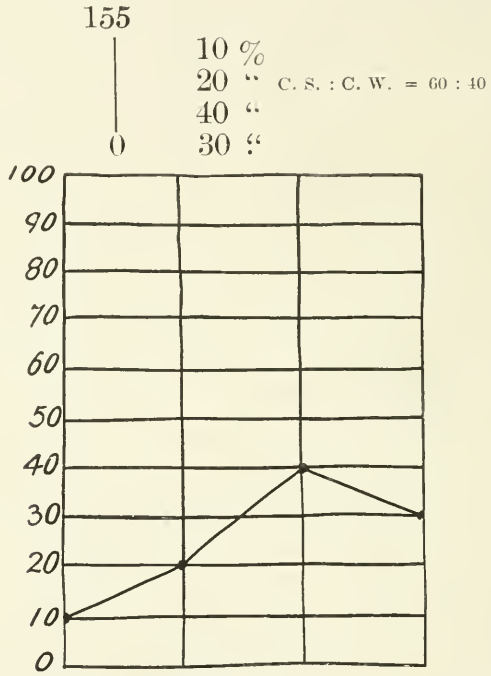

CHART IX.—Aortic regurgitation. Compensation fair, heart muscle in better condition.

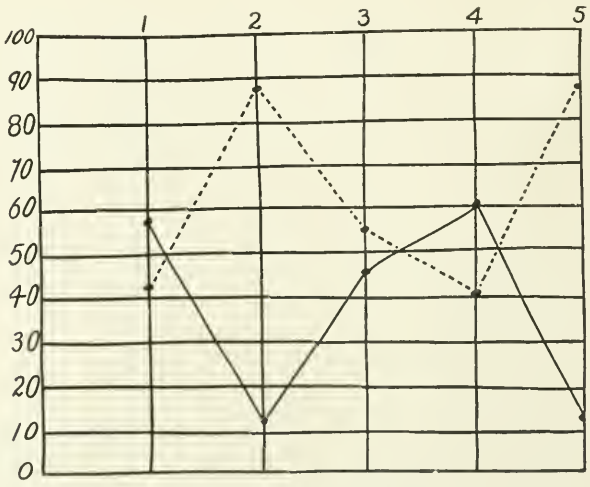

CHART X.—Aortic regurgitation.

240 — 135

14 %
33 "
9 "
43 "

C. S. : C. W. = 42 : 57

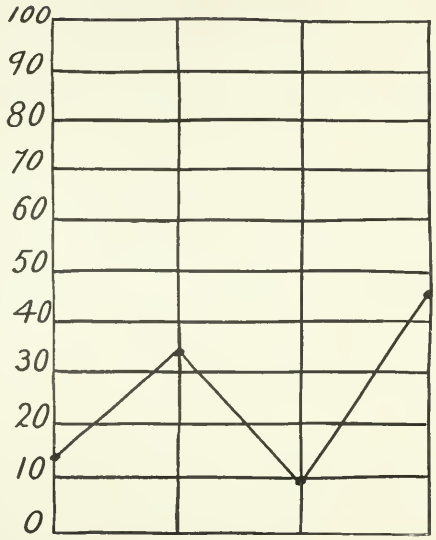

CHART XI.—Arteriosclerosis. Uncompensated single sequence.

225 — 130

7.3 %
24.2 "
63.1 "
5.2 "

C. S. : C. W. = 87.3 : 12.5

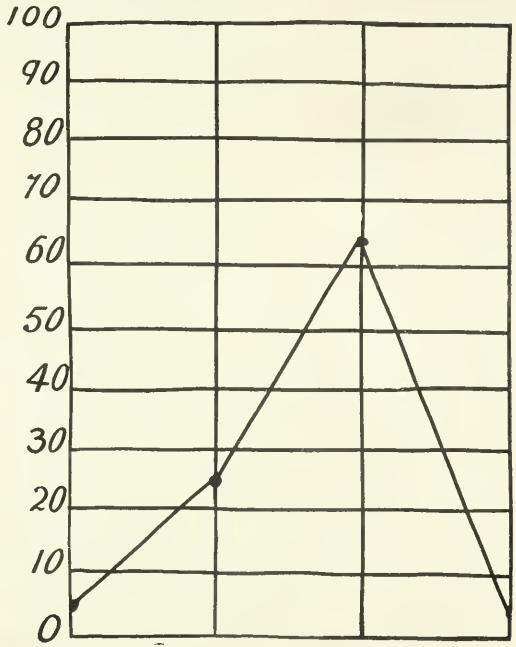

CHART XII.—Arteriosclerosis. Compensated single sequence.

ARTERIOSCLEROSIS.

This patient, a man, aged sixty-eight years, was referred to us from the eye dispensary, where he had gone for dimness of vision of both eyes. There was an enormous enlargement of the heart to the left and a moderate hypertrophy to the right. The arteries were markedly sclerosed, and later examination revealed a chronic diffuse nephritis with induration.

On admission the functional activity of the heart was not at its best, and for want of a better term we have said the heart was decompensated.

In arteriosclerosis the third phase is long, but here, owing to cardiac decompensation, it has become short. (Chart XI.)

When compensation set in the curve changes, and here the characteristic lengthening of the third phase is seen (Chart XII).

The course of the disease is well represented by Chart XIII.

The indication which we sought to meet was the high blood pressure, and, in addition to rest, bland diet, etc., we placed him on large doses of sodium nitrite and nitroglycerin. The first visit we were unable to determine his blood pressure, it being 260+. There was a gradual fall from this figure to No. 7 (Chart XIII), when the pressure reading was:

202		
183	20 per cent.	
147	38 "	C. S. : C. W. = 56 : 44.
130	18 "	
108	24 "	

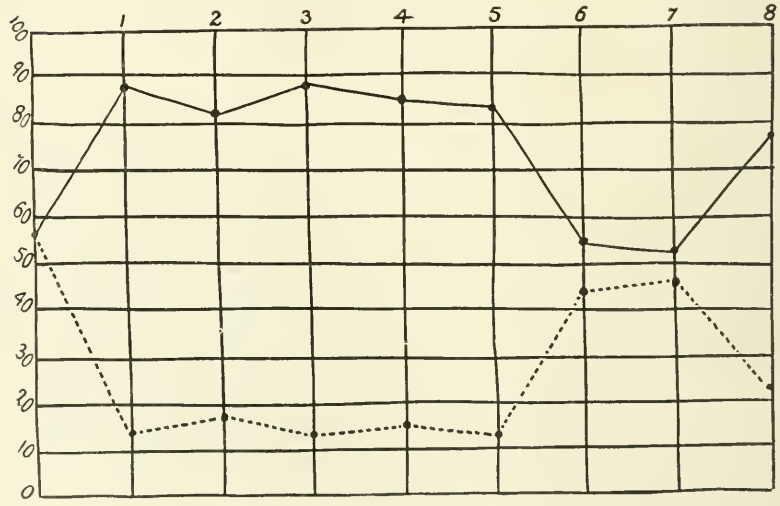

CHART XIII.—Arteriosclerosis.

On this day, as seen on Chart XIII, the two lines approximate, and the patient felt weak, "played out," no ambition for physical or mental effort, and the task of coming to the dispensary had depressed him more than at any other time. The nitrites were immediately discontinued, and no medication was given, and the next week (No. 8) the patient was improved and the blood pressure had gone up slightly.

No. 8.

209

17 per cent.
28 " C. S. : C. W. = 78 : 22.
50 "
5 "

116

We cannot refrain at this point from emphasizing the importance of controlling, by blood-pressure estimations, medication given to combat high pressure. In cases of hypertension the cardiovascular system has readjusted itself to altered conditions, and the normal, for them, is a pressure far exceeding the normal as given by us in Chart I. The injurious effect, or what would ultimately have been an injurious effect, is shown graphically in Charts X and XII, when, with the reduction of blood pressure, cardiac function was materially impaired.

In the case of the patient from whom Charts XI, XII, and XIII were plotted, the blood pressure was normal at about 220, or, in any case, subjectively he was best with that pressure, and with that pressure the factor was obtained of C. S. : C. W. = 87.3 : 12.5. When the pressure fell below that point, the ratio of C. S. to C. W. became altered in favor of the latter, and the patient felt what is best described by the German word "Matt," and we believe he was on the verge of a vasomotor collapse, and that to have reduced the pressure still farther would have been accompanied by serious consequences. The point is not sufficiently recognized that, owing to the gradual increase of blood pressure, each individual readjusts his cardiovascular physiology to compensate this, and the physiological limit is now, not 130, but may be as high as 220, as in our case. To reduce pressure below this new physiological limit is not only not indicated, but bad therapy, and hence we reiterate that with cardiac depressor drugs, or with vasodilator measures, blood pressure must be constantly watched with the sphygmomanometer.

CHRONIC NEPHRITIS.

Charts XIV, XV, and XVI represent three successive sequences taken on different days in a patient showing no circulatory symptoms. They illustrate the effect of the anemia in lengthening the second

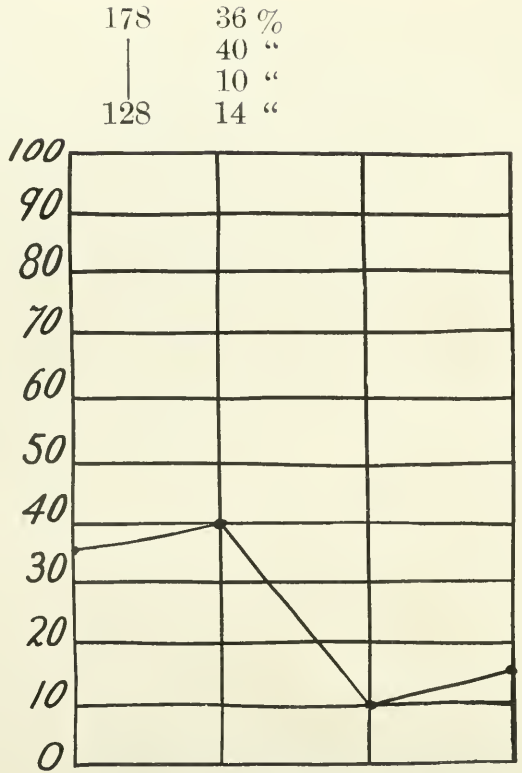

CHART XIV.—Chronic nephritis (anemia).

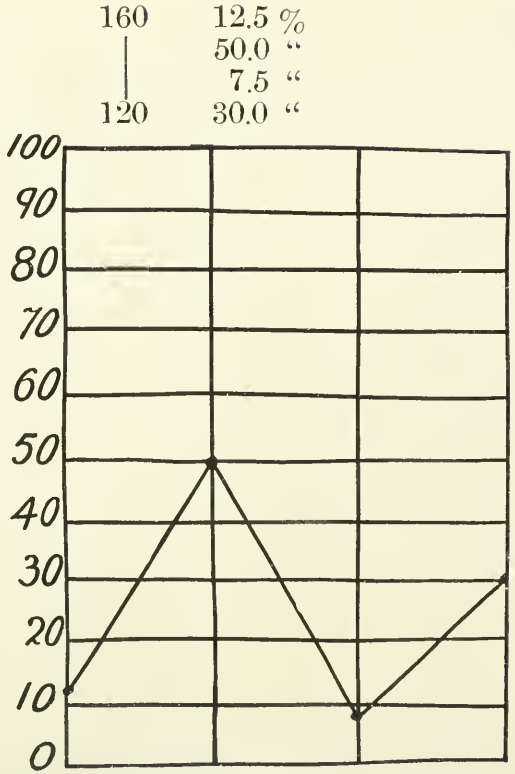

CHART XV.—Chronic nephritis (anemia).

phase. We said above that arteriosclerosis was accompanied by a particularly loud, long, third phase, and it is of interest to note here that despite some arteriosclerosis the second phase is longer than the third, due, we think, to the good functional state of the heart and to the anemia.

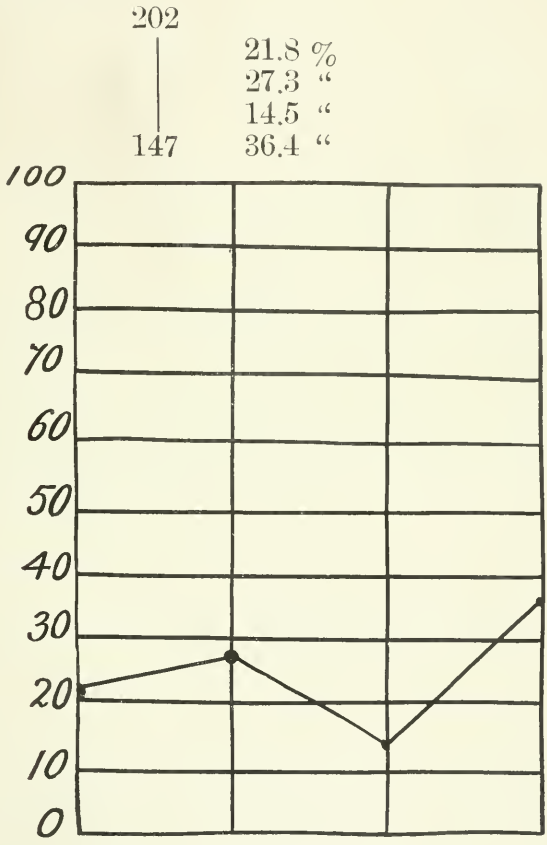

CHART XVI.—Chronic nephritis (anemia).

MYOCARDITIS.

In cases of organic disease of the heart, where the function is impaired, as in myocarditis, the sequence readings may show no phases, or one phase may be lacking, usually the second or third, and with these changes tonal arrhythmias are quite easily detected. In distinction to the functional disturbances without any apparent organic lesion, the so-called cardiac neuroses (see above), there is no variation in successive systolic and diastolic readings, which we believe to be characteristic of the neuroses.

Case I.—Katharine D., aged fifty-five years.

170
160
A few murmurs alternating with tones. The tones were weak, but fairly clear in quality.
110

Case II.—John W., aged sixty-three years.

157
No second phase.
90
85

Arrhythmia as to time, none as to intensity.

Case III.—E., male, aged twenty-five years.

110
100 Murmurs and tones alternating. No third phase.
80
65

We feel that the auscultatory method of determining blood pressure has a large field of usefulness, and that by observing the phases and their relation to one another in each sequence reading, much may be learned of diagnostic, therapeutic, and prognostic interest.

DIFFUSE SELECTIVE SCLEROSIS OF THE SUPERFICIAL VEINS.

By Harlow Brooks, M.D.,

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The selective tendency for definite systems or groups of trunks which is manifested in arteriosclerosis has long been recognized, and usually the change is most marked or sometimes even limited to a certain group of vessels. In some instances this selection seems to be determined by the nature of the exercise or occupation; thus, for example, we expect it to be most evident in the peripheral trunks in athletic or physical workers, and more advanced in the vessels of the central nervous viscera in those chiefly engrossed with nervous problems, even though the probable direct etiological factor be such a general one as a toxemia or syphilis. In other cases, however, the selective tendency appears to be due to the character of the cause or the route of its excretion; for example, in alcoholism we all recognize the frequency of involvement of the renal and hepatic vessels.

No less frequently, in my opinion, only less obviously, is this selective tendency shown in sclerosis of the veins. It is often rela-

tively quite as evident here, and it occasionally becomes even more suggestive and striking, since the veins are usually much less liable than the arteries to this type of lesion. This fact is most likely chiefly due to the lesser pressure to which these trunks are habitualy subjected. This assumption is, I think, quite warranted by the relatively more frequent occurrence of venous sclerosis in the various long trunks, notably in those of the lower extremities, which during the erect posture of the body have a far greater pressure to sustain than the veins of other distributions, and are associated during exercise with constant mechanical shocks, which probably cause minor traumatic changes in the thin walls of the venous trunks.

I believe that the following case of selective venous sclerosis is of peculiar interest, since it occurred in an individual very young for the development of any form of vascular sclerosis, and especially because of the definite selective tendency manifested in this instance for the superficial veins of the peripheral distribution, with no evidence of other venous or of arterial involvement.

The patient was a well-formed, rather sparely built boy, aged eighteen years. He was born in Austria, but for the last three years had lived in and around New York.

He entered the City Hospital with the chief complaint of pain in the left leg and thigh, so severe that he was unable to walk. The veins were stated to be hard and swollen.

The family history was practically negative; there was no history of ancestral alcoholism, gout, or syphilis.

The patient was a waiter by occupation, but had worked at this but a little over a year, previous to which time he had no regular work, but attended school most of the time. He had never done heavy physical exercise and had never been inclined toward sports involving this. He believed that he was healthy as a child and remembered no time when he was confined to bed on account of illness, except for a slight attack of "pneumonia" and for several mild attacks of tonsilitis and pharyngitis. There was specifically no history of rheumatism, gout, malaria, typhoid, or of previous venous disturbances. Of late he had used alcohol moderately, perhaps a couple of glasses of beer daily.

About one month ago, after a night spent in the society of a vigorous young woman, the patient noticed some pain and swelling with local redness on the inner side of the left leg. He went on working, and for three days paid no particular attention to it, when he found that the swelling extended and the pain became so intense that he was forced to seek aid, having first attempted relief by rubbing the parts with various medicaments, such as vaseline and alcohol. No relief followed this local treatment, and after the third day he entered my service at the City Hospital.

On examination, he was found to show a complete thrombosis of the left internal saphenous vein, extending from 8 cm. below

Poupart's ligament down to the ankle. The course of the vein was marked by a hard cord bordered on either side by an indurated and tender red band. Considerable edema, especially about the ankle, was present and he suffered exquisite pain, particularly on movement. A circular point of sharply localized bluish discoloration was found over the vein just below the knee-joint, evidently a gangrenous area. Aside from this, no lesions of importance were demonstrable on physical examination except that the superficial veins of the entire body, notably those of the extremities, were prominent and palpably thickened. The hands were constantly cyanosed, and if allowed to hang down, soon became edematous. Moderate exertion caused facial cyanosis of a peculiar mottled quality; areas of edema also occasionally developed over the face.

Examination of the heart, which was conducted with particular care and on many occasions, revealed nothing of importance; it was regular, no murmurs were present, and no disturbances of rhythm. The pulse rate varied, according to posture, condition of excitement, or after exercise, from 82 to 100 per minute, and no arterial thickening could be made out. No change in the retinal vessels, either veins or arteries, was apparent.

The blood pressure chart showed on admission a systolic pressure of 120 mm. Hg, which subsequently went up while the patient was still in bed to 140 mm., slowly falling under treatment to 110 mm. Hg. The temperature varied while under observation from 97° to 99.2°, being mostly at the normal level.

The urine was entirely normal throughout, and no conditions suggestive of either renal or hepatic disease were found.

The blood examinations showed little of importance and varied but little from the condition first found, which was as follows: Hemoglobin, 70; red blood corpuscles, 5,456,000 per c.mm.; white blood corpuscles, 7200 per c.mm. Differential leukocyte count: Polynuclear neutrophiles, 68.5 per cent.; large lymphocytes, 1 per cent.; eosinophiles, 1 per cent.; small lymphocytes, 21.5 per cent.; transitionals, 7.5 per cent.; basophiles, 0.5 per cent.

The coagulation time, as determined by the Biffi-Brooks instrument, showed considerable reduction, varying from two and one-half to three minutes.

Blood cultures were negative.

The Wassermann reaction, at this time little understood, was not tried.

There were absolutely no signs or symptoms suggesting faulty deep visceral action of any kind.

The patient, greatly to his discomfiture, was kept in bed. The leg was wrapped in cotton moistened with 33 per cent. alcohol and citric acid, and potassium iodide was administered internally.

Shortly after entering the hospital the gangrenous spot sloughed out, leaving a circular perforation 7 mm. in diameter and 1 cm.

deep, this quickly granulated up and rapid absorption of the clot in the thrombosed vein took place, although up to the time of his discharge circulation through it was not fully reëstablished. The patient gained some two or three pounds in weight while under treatment, and left the hospital after three weeks, walking, and, aside from the thickened veins, apparently well.

Briefly, the chief features presented by this case were, a diffuse, isolated sclerosis of the superficial veins, with phlebitis and thrombosis of one.

This condition is remarkable in that the sclerosis was apparently limited to the superficial veins, and was certainly relatively much more marked in them than in the other veins or the arteries. Although the coagulation time of the blood was considerably reduced, and in accordance with experiments conducted by Crowell and myself,[1] I believe that this favored the thrombosis; the chief factor back of it was the markedly altered, and in this instance clearly sclerotic alteration in the walls of the veins.

With no other evidence at hand, and the case was most carefully studied in all its aspects, it seems most likely that this selective venous sclerosis was induced by syphilitic infection either congenital or early contracted. The very early age of the patient and his apparent freedom from other lesions, which might be considered as causative in nature, direct one by exclusion toward this diagnosis, although no direct evidence of its accuracy can be advanced. We know that in syphilitic arteritis, a condition much more frequent and much more fully studied, this selective tendency toward the involvement of certain specific vascular distributions has been well established, and in my opinion it may with equal force be directed to the explanation of this unusual instance of diffuse superficial venous sclerosis occurring in youth.

RETROBULBAR NEURITIS AS AN EXACT DIAGNOSTIC SIGN OF CERTAIN TUMORS AND ABSCESSES IN THE FRONTAL LOBES.

By Foster Kennedy, M.D., B.Ch. (Queen's),

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The diagnosis of tumor and abscess formation in the frontal lobes has for long been a matter of very considerable difficulty, owing to the paucity of definitely known centres in these areas;

[1] Journal of Experimental Medicine, 1908, vol. x, No. 2.

we have been compelled to look for our main guidance to the effects of pressure exerted backward on either the pyramidal tracts or their cortical origins; and to the existence of some abnormality of mental state as a more or less confirmatory factor. It will readily be seen that, valuable as these phenomena may be, when judiciously and skilfully considered, they may be at times but sorry sign-posts, and any concrete indication by which we may be able to augment them must be welcomed as a valuable addition to our ability to diagnosticate and treat these conditions.

It is the purpose of this paper to consider, in some detail, the various subjective and objective signs in a series of 6 cases of expanding lesion of the frontal lobes. In 5 of these the accuracy of the diagnosis was proved by operation. In the sixth, a palliative decompression operation only was attempted, in consequence of which procedure the tumor was not seen; nevertheless, the propriety of including it in this series will not be questioned when it is realized how completely it coincides in symptomatology with its fellows.

The 6 cases to be considered in this paper are set thus in series, for the reason that, in each, there is shown a symptom complex which, if looked for, is easily discoverable, and which is decisively diagnostic, in that it cannot possibly be simulated by any lesion failing to exert pressure on the inferior surface of one or other frontal lobe.

This sign to which I wish to draw attention is the occurrence of true retrobulbar neuritis with the formation of a central scotoma and primary optic atrophy on the side of the lesion, together with concomitant papilledema in the opposite eye.

One may say that if there be no doubt that a given patient has a brain tumor, and if that patient develops a unilateral retrobulbar neuritis, then it is certain that the tumor is situated in the lower part of the frontal lobe on the same side as that on which the retrobulbar neuritis and primary optic atrophy have occurred.

Before discussing the mode of production of these phenomena, it may be well, in a few sentences, to consider some important points in the structure and pathology of the optic nerves. Both developmentally and anatomically they form a part of the central nervous system; their constituent fibers take origin in the ganglion cells of the retina; like other central fibers, they are without primitive sheaths, and in consequence, when once destroyed, they are incapable of regeneration. The sheathless fibers maintain fairly definite relative positions in their course through the optic nerves, and it has been found that fibers originating in the macular region of the retina lie as a wedge-shaped bundle toward the outer side of the nerve, the apex of the wedge being directed mesially while the base is covered completely by fibers coming from retinal areas other than the macula.

This macular bundle subserves central vision; physiologically

more delicate than its fellows, its structure presumably is proportionately more fragile; the result being that direct pressure on the optic nerve has, as a first consequence, a deterioration of function, and later, a primary atrophy of the macular fibers with loss of central vision; and this in spite of the fact that the grosser strands retain functional activity, though subjected by their peripheral position to more immediate and direct trauma.

The sequence of events just described is that which takes place when, from the earliest inception of disease, one or other optic nerve be directly subjected to pressure. If, however, the expanding lesion be situated in the substance of the frontal lobe, not implicating at first the underlying optic nerve, but producing a general rise of intracranial pressure, there will be brought about a bilateral papilledema without central scotoma, or loss of visual acuity.

The tumor or abscess expands until at last it presses directly on the upper surface of the ipsolateral optic nerve. The following phenomena will then result: The papilla contralateral to the tumor will remain edematous and visual acuity in that eye will, for a considerable time, remain good. In the ipsolateral eye edema will rapidly subside and visual acuity will quickly diminish, a central or paracentral scotoma will develop, and in a few days time, well-marked temporal pallor will be seen opthalmoscopically, an expression of atrophy, which, at a later period, will be observed in all four quadrants of the disk.

In order properly to understand the mechanism of these occurrences, it is necessary to review the methods by which a general rise of intracranial pressure results in optic neuritis, or, to use the much better term suggested by de Schweinitz, papilledema. There have been many theories on this subject. Hughlings Jackson and Brown-Séquard put forward a somewhat vague hypothesis which has been called the "reflex irritation" theory, which alleged the papillary changes to be the result of certain nutritive alterations in the walls of the intracranial bloodvessels produced by the presence of a foreign body in the cerebral substance. By others, a slight, basal meningitis has been thought to be constantly co-existent with neoplasms, from which meningitis, an inflammatory process, descends along the optic nerve coverings to find its ultimate expression as a papillary neuritis. A third theory argues for an intense cerebral edema communicated directly to the papilla of the trunk of the optic nerve.

It is beyond the scope of this paper to discuss the merits of these various contentions, all of which find some champion even at the present day. The explanation which most fully satisfies conditions is supported by sound evidence at once anatomical, pathological, and therapeutic, and may be designated the "mechanical" theory of papilledema.

In support of this view the following facts may be cited: (1)

The space between the optic nerve and its sheath is directly continuous with the intermeningeal spaces about the brain. (2) When intracranial pressure is raised, an excess of cerebrospinal fluid is forced into the intervaginal spaces of the optic nerves; a resultant edema is thus created around the nerve heads. This distention of the intervaginal sheaths may easily be demonstrated by autopsy in cases where papilledema has been seen clinically. (3) The occurrence or non-occurrence of papilledema in cases where intracranial pressure is raised is dependent in the highest degree upon the formation of the eyeball; in hypermetropic and emmetropic eyes the ocular ending of the vaginal space is directed sharply *toward*, and in myopic eyes *away from*, the optic nerve, an arrangement which, in the latter condition, results in an infiltration of the fluid contained in the sheath through the sclera, while in the former the nerve head becomes speedily edematous. (4) Decompression operations producing a diminution in an increased intracranial pressure are followed by a corresponding diminution in the degree of papilledema present.

These considerations make clear the method by which a constriction placed on an optic nerve in which papilledema has already occurred is capable of abolishing that papilledema and substituting for it what may accurately be termed a primary optic atrophy.

The optic nerve lying below the frontal tumor or abscess, together with its fellow on the opposite side, is in a condition of papilledema the result of generally raised intracranial pressure. As we have just seen, the nerve fibers are intact and the sheaths are distended with fluid, the papillæ, in consequence, being swollen and edematous. The superjacent foreign body grows until it at last presses on one of the optic nerves, the sheath of which becomes constricted so that the passage of fluid from the intracranial cavity to the nerve head is prevented. The excess of papillary fluid and that contained in the optic nerve sheath distal to the constriction then disappears by filtration and absorption; that is, the opthalmoscopic appearances of papilledema vanish and, as the pressure on the optic nerve becomes more pronounced, the various phenomena associated with retrobulbar neuritis become manifest.

Owing to the proximity of the olfactory bulbs to the optic nerves, we would expect that trauma to the latter would inevitably produce damage to the former, and, as will be seen in the following cases, depression or loss of the sense of smell is practically always found on the side on which retrobulbar neuritic atrophy has occurred. It is not intended to discuss in detail the other signs of frontal lobe lesions which were present in these cases; the mental state in which a trivial and meaningless jocosity predominates, the tremor in the hand ipsolateral to the tumor, nor the signs of gradual compression of the pyramidal tracts going to the opposite side of the body. These things have been fully dealt with by other observers, and their

presence will be indicated in the case reports. Nor is it wished to becloud the diagnostic importance of the sign which has just been discussed and which is the main purpose of this paper.

The first case is that of a woman, aged thirty-seven years, who, in September, 1908, was admitted to the National Hospital, Queen Square, London, to the service of Sir William Gowers, who has kindly allowed me to make use of my old notes.

The history was briefly as follows: For many years she had been subject to fainting attacks of more or less prolonged duration. In all other respects her previous health had been good. In October, 1906, she began to suffer from headaches of increasing severity, with marked fatigue. One evening, after considerable exertion, she fainted and remained unconscious for two hours, after which she had a severe vomiting attack, which lasted for a whole night.

During 1907, headache, nausea, and vomiting increased, and in June of the following year she began to have transient blurring of vision in the left eye, and later some weakness slowly developed in the left arm and leg. She came into the hospital in September, 1908. Her mental condition was normal. Nutrition was good. The sense of smell was completely absent on the left side, while on the right, though at first normal, in the course of six weeks it became lost.

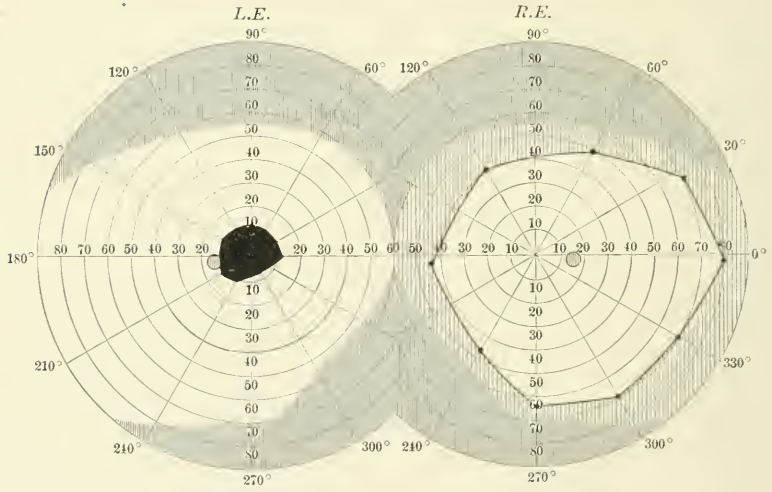
The left optic disk was clear, its edges were sharply outlined, the physiological pit was not filled in, and the vessels were rather below normal in size. Its color was grayish, particularly in the temporal portion of the disk. The right disk offered a striking contrast, being markedly edematous to the extent of 5 diopters; the edges were completely obscured, the veins were enlarged, and the amount of retinal exudate was considerable. Visual acuity in the left eye was markedly depressed. Jaeger test types could not be read, and under observation, vision rapidly retrogressed, so that light perception was but dimly retained.

The visual acuity of the right eye was at no time less than normal, despite the high degree of papilledema present. The visual fields were as shown in Fig. 1, that is, the left eye showed the presence of a central scotoma complete for white and for colors up to 10°, while in the right there was a mild degree of general concentric contraction.

The pupils were equal, both acted briskly to light, but the contraction of the left was not sustained. It quickly dilated again, despite the maintenance of illumination, a phenomenon so characteristic that it has been called by the late Mr. Marcus Gunn "the retrobulbar reaction." The other cranial nerves were normal. There was considerable diminution in the power of the left arm and hand, and to a less extent in the left leg as well. The deep reflexes on the left side were increased; the left abdominal reflexes were diminished; the left plantar reflex was never obtained, while that

on the right was always of the flexor type. At no time was there any change in sensation.

An effort to remove the tumor was made by Sir Victor Horsley in October. The patient, however, died shortly after the initial decompression operation had been completed. On autopsy, a a subfrontal indurated endothelioma was revealed, its origin having been taken from the dura mater over the crista galli. The growth compressed but did not infiltrate the cerebral tissue, and measured in circumference about seven inches; in anteroposterior diameter, two and one-half inches, and from side to side two and five-eighths inches. It extended farther backward on the right than on the left side, by which circumstance the production of the left-sided paresis became plain. The left olfactory bulb was obliterated; the



Central scotoma, outside of which objects and colors were clearly seen.

Slight concentric contraction; no central scotoma.

Fig. 1.—Visual fields of Case 1.

left optic nerve was directly pressed upon; there was no distention of the left optic nerve sheath, whereas the lumen of that on the right side was markedly enlarged. A careful microscopic examination of the optic nerves was made by Mr. Leslie Paton, who found in the left a "compact fasciculus of degenerated fibers in the outer part of the nerve."

My second case is that of a man, aged thirty years, who was admitted in March, 1911, to the second surgical division of Bellevue Hospital, New York, under the care of Dr. John Rogers, who kindly asked me to see the case, and to whom I am indebted for permission to make use of the following notes.

A bartender by trade, he had been struck on the right frontoparietal region by a spent revolver bullet in the course of a saloon

squabble in July, 1910. The bullet embedded itself in the bone but failed to penetrate the skull cavity; it was easily removed within a few hours of the injury, and the wounds caused by trauma and operation quickly healed. The man resumed his occupation shortly afterward. He remained in perfect health until February, 1911, when he began to complain of headache of considerable severity. He became moody and irritable and so changed in disposition that his relatives brought him to Bellevue Hospital, where he was admitted, as I have indicated, some three weeks after the appearance of symptoms. I saw him two days later, when his condition was briefly as follows: Mentally, he was clear and well orientated. A feeble jocosity of manner regarding our interest in him and the details of the examination might or might not have had pathological significance. The olfactory sense, while not lost, was definitely depressed on the right side. The pupils were normal in appearance and reactions. The right optic disk was quite clear. Its color was good, though the vessels seemed to be rather below normal in size. The left disk was completely obscured by swelling. Both veins and arteries were tortuous and congested and much exudate and many hemorrhages were visible, both on the disk surface and the adjoining retina. Visual acuity in this eye was normal. He complained of "blurring of the sight" of the right eye, but no scotoma could then be made out. Very slight facial weakness on the left side; when the eyes were closed tightly the left eyelash was always less well covered than the right. Power in the hands and arms was equal on the two sides, but there was a well-marked, rather coarse tremor in the right hand while held outstretched. Dorsiflexion of the left foot was less well performed than on the right side. The left abdominal reflexes tired before those on the right; the left knee-jerk was brisker than the right; the left plantar reflex was of indefinite character, while the right was invariably of flexor type. Sensation was normal.

The picture thus presented was that of an expanding lesion of the right frontal lobe.

The history of trauma and the rapidity of the onset of the symptoms made the theory of abscess more probable than that of tumor, but it seemed wise to have the cerebrospinal fluid examined before operating. This was done. It was disconcerting to hear that there was neither leukocytosis nor lymphocytosis in the fluid and that the Wassermann reaction in the fluid was strongly positive, a report which, coupled with another to the effect that the opthalmoscopic conditions in the left eye were the result of syphilitic neuroretinitis, seemed almost irrefragable proof that the patient was suffering not from cerebral abscess, but from general paresis. There was no history of syphilis.

The progress of events in the following ten days showed where lay the truth. Swelling and exudate increased in the left eye, the visual

acuity of which remained perfect, an impossible condition of affairs were the retinal elements themselves diseased to the degree shown by the opthalmoscope. Visual acuity rapidly sank in the right eye and a central scotoma, complete at first for colors and then for all objects, became easily demonstrable.

A few days after the presence of the scotoma became certain, a well-defined crescent of pallor became obvious on the temporal side of the otherwise normal right papilla. The sense of smell became almost completely abolished on the right side. The left hemiplegic signs became more and more evident, at first slowly, then more and more rapidly, until, on the day of operation, paralysis of the left arm and leg was almost complete.

On March 28 Dr. Rogers operated. An immense abscess was found to occupy the entire right frontal lobe; between 8 and 10 ounces of staphylococcal pus were evacuated and the cavity was drained. Recovery was exceedingly rapid. Two weeks after operation the patient was up and walking about the wards and balconies, with some increase of the deep reflexes on the left side as the sole trace of his recent hemiplegia. The central scotoma in the right visual field completely disappeared, and what is, perhaps, more remarkable, the pallor which had been observed in the temporal portion of the right optic disk gave place to the rosy pinkness of a healthy papilla.

My third case is that of an unmarried woman, aged forty-two years, who was admitted to the National Hospital, London, in March, 1909, to the service of Dr. Risien Russell, by whose courtesy I am enabled to state the following:

Toward the end of 1906 the patient began to complain of occasional dizziness and "queer feelings" in the head. In May, 1907, she had a slight generalized convulsion during sleep, which in no way incapacitated her for work (clerking) on the following day. From that date until December, 1907, when she had a second slight convulsion, she was troubled with frequent headaches, and petit mal attacks. In August, 1908, headache began to be violent, and when most severe was often accompanied by transient blindness in the right eye. Nausea then became constant and vomiting frequent. In March, 1909, vision became very rapidly dimmed, and the fundi were examined, as a result of which she was admitted to the Queen Square Hospital.

Her mental condition was apparently normal. The sense of smell was abolished on the right side, and much diminished on the left. Vision on the right side was reduced to $\frac{3}{60}$ and on the left to $\frac{3}{36}$. A central scotoma, complete for colors and objects was found in the right visual field; the left field showed a marked degree of concentric contraction, but no scotoma (Fig. 2).

Fundi. Left eye: Intense papilledema with numerous hemorrhages. The highest point of swelling could be seen clearly with a + 8

diopters lens, but this reading was reduced to + 6 diopters by reason of the presence of + 2 diopters of hypermetropia.

Right eye: The optic disk was very pale, with clearly cut margins. The physiological pit was seen distinctly. The vessels were below normal in size.

There was considerable weakness of both external recti muscles. Beyond slight weakness, of supranuclear type, of the left side of the face, together with increased deep reflexes on the left side, the patient did not present any further signs of localizing value.

A right-sided temporal decompression operation was performed by Mr. Donald Armour, which resulted in cessation of headache, nausea, and vomiting. Swelling disappeared from the left disk, to which eye normal visual acuity was restored. In this case

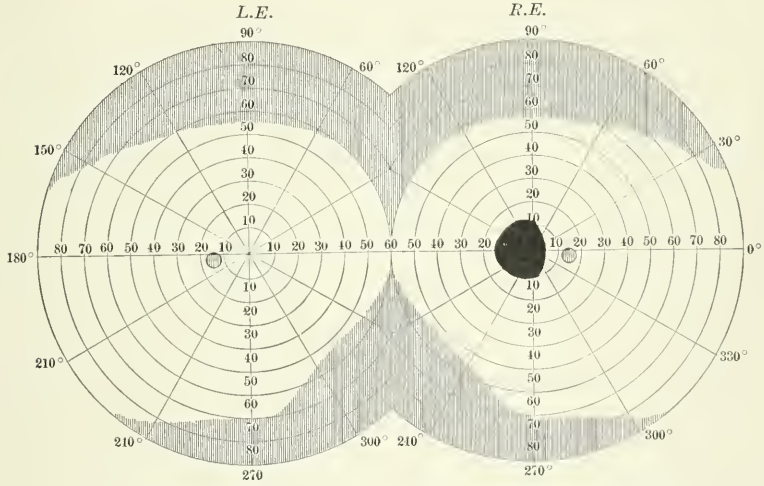


Fig. 2.—Visual fields of Case III.

however, operation had no effect on the atrophic condition of the right optic nerve. Nine months after operation the right papilla was pearly white in color and perception of light was only possible in the periphery of the right visual field, showing that the reduction of the general intracranial pressure had failed to have any effect on the local pressure exerted on the trunk of the right optic nerve.

These three cases are classed together because in each retrobulbar neuritis occurred in the nerve ipsolateral to the tumor before papilledema had had time to develop; that is, direct pressure was exerted on the nerve trunk from the very beginning of the disease. The next three cases show a somewhat different picture. Here no local pressure was exerted on the optic nerves until after the occurrence of bilateral papilledema. When local pressure eventually did occur,

the appearances due to retrobulbar neuritis were substituted for those due to papilledema.

The first case in this subdivision is that of a schoolmaster, aged thirty-seven years, who was admitted to the National Hospital in June, 1909, in the service of Dr. T. Grainger Stewart. For two years before coming under observation he had suffered from progressively severe headaches, frontal in position and paroxysmal in type. In January, 1908, he had a sudden attack of unconsciousness with general tonicity and cyanosis, followed by a considerable slurring in speech, which latter, however, passed off in a day or two. From that time he was subject to such seizures every two or three weeks; in addition, there were momentary lapses of consciousness of typical petit mal character which occurred still more frequently. Nausea was frequent, but there was never any vomiting.

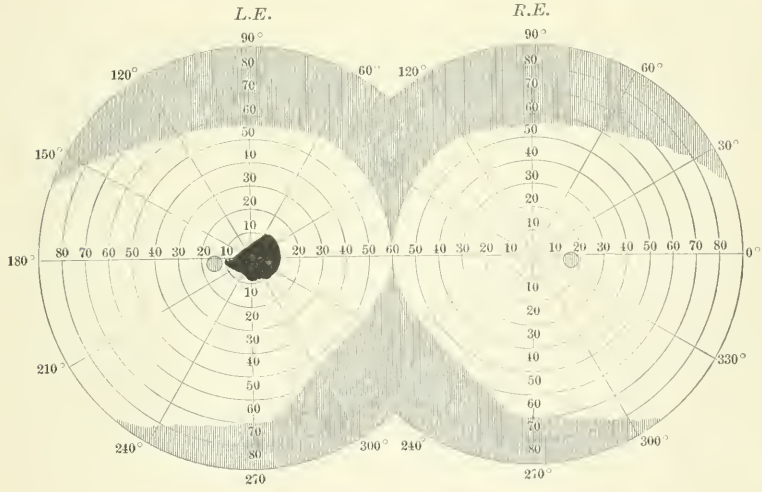
In May, 1909, he began to be unsteady in walking, and considerable tremor developed in both hands. On the evening of the day on which he was admitted to the hospital he had a convulsion, which occurred during the course of my examination. He began to tremble all over, became cyanosed and slightly rigid, and lost consciousness. The corneal reflexes were abolished. The coarse tremor, which was more pronounced on the right side, continued during the two minutes of unconsciousness. After the attack there was an almost complete temporary right hemiplegia, with a passing difficulty in speech.

On examination, the patient had the appearance of one suffering from intense intracranial pressure. Attention was very defective, answers to questions were often quite irrelevant, and there was much drowsiness and frequent yawning. Patient was unable with either eye to read the largest letters on the test card. The sense of smell was markedly diminished on the left side, and was normal on the right. The right optic nerve was the seat of a steep-edged edema, the highest point of which was seen with a + 6 diopter lens. There were numerous hemorrhages on and around the papilla. The left optic disk showed a crescentic pallor in its temporal part. The physiological pit was filled in, but no swelling could be measured on the disk surface. The papillary edges were clear, but irregularly waved in outline; there was intense disturbance of choroidal pigment. Vessels were below normal in size. There was considerable weakness of supernuclear type of the right side of the face. The right arm and leg were definitely less strong than their fellows of the opposite side. The right abdominal reflexes were depressed as compared with the activity of those on the left. The knee-jerks were equal; the left plantar reflex was invariably of the normal flexor type; that on the left side was frequently not obtained, and when present was sometimes of flexor and sometimes of extensor type. There was no sensory change. The patient was frequently inconti-

nent of urine, a circumstance of which he was apparently quite careless.

On June 22 a bone defect measuring three by two and one-half inches was made by Mr. Donald Armour in the left frontal region. Intracranial pressure was extreme.

By the following day, the patient's mental condition had very greatly improved and his powers of attention had become so much better that it was possible to obtain an accurate perimetric tracing of the fields of vision. These were taken by means of an ordinary perimeter and also with a Bardsley's scotometer; the results obtained with the former failed to show any concentric or hemianopic contraction, but those obtained with the latter showed a cleanly cut central scotoma in the left visual field, complete both for colors and objects (Fig. 3).



Central scotoma. No central scotoma.

Fig. 3.—Visual fields of Case IV. Perimetric tracing taken with a Bardsley's scotometer.

The second stage of the operation was carried out after a week's interval. The left frontal lobe was completely exposed. None of its surfaces was the seat of tumor formation. A large horizontal incision was made in the lobe, which was explored with the finger. Lying deeply near the middle line there was found a thick grayish mass, which, on being opened, proved to be a cystic wall containing yellow gelatinous material. The growth was poorly defined, but apparently all of it was removed by spoon and finger.

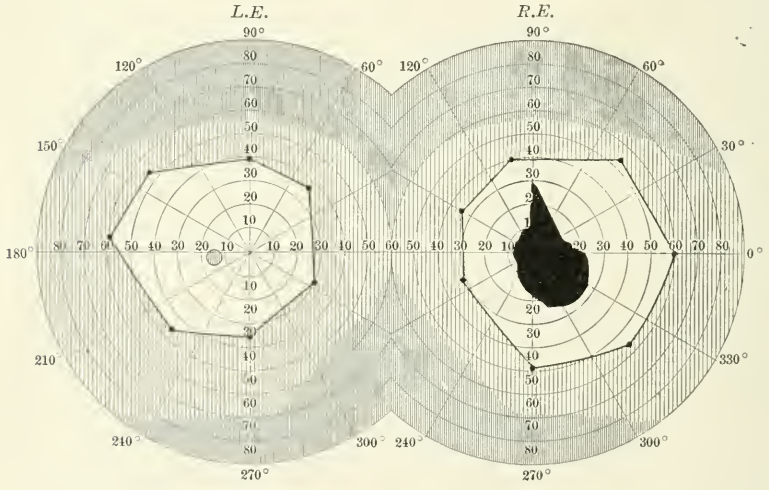
On the evening of the day of operation, the patient moved both the right arm and leg strongly, and showed no evidence of aphasia.

He made an uninterrupted recovery and left the hospital on January 3, 1909, with very slight weakness of the right limbs, the

plantar reflexes, however, being both of the flexor type. His mental condition on discharge was apparently normal.

The second case is that of a woman, aged thirty years, whom I saw in the service of Sir William Gowers, in November, 1909. She had been subject to fainting attacks since the age of seven. These seizures never possessed any of the characteristics of major epilepsy. In the summer of 1906 she began to suffer from frontal headaches,which in the next two years became very severe and were occasionally associated with transient dimness of vision, especially in the right eye.

On admission to the hospital, she stated that in August of that year (1909) she had had such a cold in the head that in ten days' time she had completely lost the power of smell in the right nostril, and vision in the right eye had so much deteriorated that she was only



Concentric contraction; no scotoma. Concentric contraction with central scotoma.

Fig. 4.—Visual fields of Case V.

able to make out the forms of large objects with that eye. This was the acuity of vision in the right eye, while that in the left had also become reduced to $\frac{2}{60}$.

A large central scotoma was found in the right visual field, together with considerable concentric contraction; the latter was also present in the left perimetric chart, but no central defect could be made out (Fig. 4). Ophthalmoscopic examination showed on the left side marked swelling of the papilla, +3 diopters in height. The color of the disk was markedly deeper than normal, and the retinal vessels were swollen and tortuous. The right papilla was edematous to an identical degree. The disk, however, was intensely white in color, and the caliber of the arteries was very markedly reduced. There was complete anosmia on the right side and considerable deterioration

of the sense of smell in the left nostril. A coarse rhythmical tremor was seen in the right hand when the hand was outstretched. The deep reflexes on the left side were increased, the left abdominal reflexes were depressed, and both plantar reflexes were of the normal flexor type. Her mental condition was distinctly abnormal; she was very excitable, laughed foolishly and causelessly; joked feebly and inappositely; was very ready to take offence, and, on the other hand, was effusively apologetic over trifles. There was no speech defect.

On November 23, 1909, Sir Victor Horsley made a large osteoplastic flap over the right frontal region, and a week later the dura mater was incised and the right frontal lobe exposed. Intracranial pressure was greatly raised. No tumor was seen on the brain surface. A vertical incision was therefore made in the right frontal lobe, which was then explored by the finger. Deeply embedded in the brain and almost resting on the orbital plate was found a hard fibrous growth, evidently of benign character, in that it was sharply delineated from the cerebral substance. It was easily removed.

Papilledema later completely disappeared, and vision improved in the left eye.

My last case is that of an elevator runner, aged twenty-six years, whom I saw in February, 1911, in Professor Dana's service at the Neurological clinic, Cornell University Medical College, New York.

Onset of symptoms dated from six weeks before his admission to the clinic, when he began to notice dimness of vision first in the left eye, and a few days afterward in the right also. For the first week he had a little dull headache over the eyes, which, however, did not trouble him greatly, and which never recurred. Deterioration of vision was progressive, and when he came under observation he was only able to see a lighted match when held in the periphery of the visual fields of either eye. With the exception of his blindness, he felt himself to be in normal health. He gave a history of having smoked upward of a hundred cigarettes a day; his consumption of alcohol had been considerable and systematic.

On examination, it was found that he was unable to smell any aromatic substance, though ammonia was at once appreciated and recognized; he had complete anosmia in both nostrils. The pupils were equal and acted briskly to light and on convergence, the contraction, however, in each case being poorly sustained.

Ophthalmoscopic Examination. Right eye: The optic disk edges were blurred; no venous engorgement nor tortuosity. The papillary color was about normal. No hemorrhages nor other exudate seen. The left ocular fundus showed a similar picture, with the exception of the fact that the optic disk on that side was definitely blanched, especially in its outer portion. The visual fields were as indicated above.

The right abdominal reflexes were absent, while those on the left side were obtained but once. The right cremasteric reflex was diminished. The knee-jerks were very active, the right being greater than the left. There was also an ill-sustained right-sided patellar clonus. Both of the plantar reflexes were of the flexor type.

The association of papilledema, anosmia, and pathological reflexes on the right side led to a diagnosis of left frontal tumor; he was accordingly admitted to the second medical division of Bellevue Hospital. When examined there, the unilateral reflex signs found in the Out-patient Department could not be obtained; repeated examinations over a period of two weeks failed to elicit any pyramidal signs whatsoever.

This failure to corroborate localizing phenomena, added to the retention of light perception in the peripheries of the fields, and the entire absence of all the usual signs of general intracranial pressure, such as headache, nausea, vomiting, or drowsiness, threw doubt on the original diagnosis and brought up the question of the fundal conditions being the result of either a toxic retrobulbar neuritis of tobacco and alcoholic origin, or of acute disseminated sclerosis.

The diagnosis of neoplasm was established by the patient having a severe generalized convulsion in the night of March 11; no sign indicative of the localization of the tumor was obtained until five days later, when the right abdominal reflexes were again depressed and the right plantar reflex was found to be sluggish with an occasional tendency toward the extensor type of response, while its fellow remained definitely flexor. It was accordingly decided to explore the left frontal lobe. On the afternoon of March 17 the patient suddenly had several general epileptic attacks, after which he passed into a stuporous condition, which rapidly deepened into coma. Dr. Woolsey rapidly exposed the left frontal lobe, the lower two-thirds of which was seen to be the seat of an enormous tumor, which was easily removed. The patient died before he could be brought back to bed.

The growth occupied, as has been said, the lower part of the left frontal lobe and pressed upon the sublying optic nerves, the left nerve being the one more directly involved. Microscopically, it was a glioma. It weighed 165 grams.

In this last case the tumor, by pressing on the optic nerves and olfactory bulbs of both sides, produced bilaterally a symptom complex seen in the other cases on one side only.

A CRITICAL REVIEW OF THE SURGICAL TREATMENT OF NEPHRITIS.[1]

By Morris Booth Miller, M.D.,

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To attempt to discuss the operative treatment of Bright's disease within the limits of a short paper is somewhat difficult, in view of the extremely interesting, and at times rather animated, controversy which has enlivened the literature on this subject during the last decade. Furthermore, it must be borne in mind that we are considering a proposition over which opinions are still widely divided and wherein the evidence has not yet been marshalled in orderly array. I shall, therefore, merely sketch in broad lines the birth of the idea that nephritis may be cured by the knife, trace in more or less fragmentary manner the determination of many of the questions which have arisen, note most briefly the results of clinical and experimental observations, and, finally, offer to you certain deductions and conclusions which may be reasonably drawn at this time. To those who prefer to seek their data at their sources I may say that Edebohls' article on "Decapsulation of the Kidneys for Chronic Bright's Disease," published in the *Transactions of the Section on Surgery and Anatomy of the American Medical Association*, 1908, furnishes a long and nearly complete bibliography.

In 1896 Reginald Harrison, in the Presidential Address before the Medical Society of London, drew attention to some cases where albuminuria and other renal symptoms, thought to have been due to stone or other operable condition, had entirely recovered after nephrotomy, though no stone had been found. The operation consisted merely of incision or puncture of the kidney with subsequent drainage. He inferred from these results that the recovery was due to the restoration of the normal renal circulation through the relief of tension and congestion. He further suggested that the recognition of tension as a factor in kidney disease had not received adequate attention, and that further study along that line might lead to some revision of our views of renal pathology. Five years later he read a paper entiled "A Discussion on Renal Tension and its Treatment by Surgical Means," before the British Medical Association, in which he urged that in nephritis, the engorgement of the renal tissues was the dominant factor, and that it might properly be relieved by incision and puncture. He called attention to the well-recognized benefit arising from operation on the testicles and pancreas to relieve tension, and argued by analogy that the kidneys

[1] Read before the Philadelphia County Medical Society, March 8, 1911

were similar fibrous-covered organs and as such might be operated on in Bright's disease. Six cases were reported, in which cure or improvement had followed operation, but apparently in none of these was the operation performed for the direct cure of nephritis.

The late George M. Edebohls, of New York, stated early in 1899 that from a series of 154 nephropexies done on 118 patients, he noted in 6 there was present chronic nephritis. In the first 5 the operation was done without thought of influencing the nephritis, but inasmuch as the improvement was so striking in 3 of these 5, he decided in the sixth case to operate for that indication alone; accordingly, on January 10, 1898, the first deliberate operation for nephritis, by decapsulation, was performed. These early cases may be briefly summarized as follows: The first showed chronic diffuse nephritis, in which only one kidney was operated on, but two months later albumin and casts had disappeared. The second was also one of chronic diffuse nephritis, but no improvement followed the operation. The third had chronic interstitial nephritis of several years' standing, and in this case there was no improvement. The fourth was suffering from chronic interstitial nephritis of the left kidney, the right being healthy; in this case the urine showed no indication of nephritis four months later, and two years after operation was well. In the fifth case a right nephropexy was done on a patient suffering from chronic nephritis (type not stated), in which recovery was complete a year later. The sixth case, the one in which the operation was performed for no other purpose, a double nephropexy was done for chronic interstitial nephritis in which only the left kidney was involved. So successful was the result that a year later the patient was pronounced entirely well. Edebohls propounded the theory that the cure in these cases was based upon a new blood supply which arose from the perinephric area and attached itself to the denuded kidney, revivifying the diseased renal tissue, and gradually restoring it to a state of health. He called attention to the fact that unilateral nephritis was more common than generally thought, a point which Mr. Harrison had also affirmed.

The medical world received the announcement that this formidable disease was curable by surgical interference with the keenest interest, and at first there was a tendency to credit surgery with another brilliant victory in the domain of internal medicine. Within a very brief period, surgeons in different parts of the world commenced to record their operative results, the terms of their observations ranging from tentative approval to glowing enthusiasm. Among the more notable men who operated for the cure or improvement of chronic nephritis, were Rovsing in Denmark, Israel in Germany, Pousson, Tuffier, Talamon, and Jaboulay in France, Giordano in Italy, Ferguson, Lloyd, Gibbons, and, of course, Edebohls in America. Experimental research was undertaken to settle the questions which were raised by this novel

proposition, and valuable work was done by Claude, Balthazard, Rovighi, Johnson, Müller, Reis, Wetzel, and others. But it was not long before the opposition began to make itself felt. Led by Senator, in 1902, who was ably seconded by his fellow Germans, Rosenstein, Kümmel, Riedel, and Zondek, and in America by Conners and Porter, came a veritable avalanche of criticism, a strenuous denial of the theories which had been advanced by the two pioneers in this field, and a general refutation of the proposition that Bright's disease could in any way be influenced by surgical measures.

In order to bring into proper perspective the subject as it stands today, I shall attempt to formulate certain conclusions from the vast material now at our disposal. In the first place, it is generally agreed that albuminuria is not *per se* an evidence of Bright's disease, although the etiological factors back of it will in time, if not removed, occasion those tissue changes in the renal substance which characterize that disease. Broadly speaking, all cases of albuminuria may be divided into two classes—those in which the cause is confined to the kidney itself and those in which the responsible factor is systemic. In the first group should be mentioned, prominently, such local causes as wounds of various kinds, renal and perirenal infections, irritation arising from stone or detritus, and very particularly all those malformations and displacements which interfere with the normal circulation. In each and every form of what may be termed local nephritis the only sound method of relief must be surgical, since with mechanical causes we require mechanical measures to accomplish a cure.

A word with reference to unilateral nephritis may be of interest at this point. In many of the earlier cases which were cured only one kidney was subjected to operation. The results were explained on the theory that Bright's disease in some instances is a one-sided affair. That this is true in the strict sense that albuminuria, due to local causes, is frequently unilateral and that if it continues over a long period structural changes may occur in the affected kidney, must be admitted. But I am familiar with no postmortem findings which would tend to confirm the suggestion that systemic nephritis is ever one-sided, and there is no reasonable hypothesis why the systemic causes of albuminuria should fall upon a single kidney. To the writer, the presence of unilateral albuminuria would seem the best evidence of a local lesion, and as such would demand investigation into the status of the involved organ by operation.

The second group of cases, namely, those in which albuminuria arises from systemic causes, present far greater difficulties when it comes to studying the theoretical and practical possibilities of surgical aid. The systemic causes may be enumerated as follows: (1) Organic and inorganic poisons from without, acting through the blood; (2) overcharging of the blood with proteids; (3) micro-

organisms acting on the living cells or on the proteids in the blood, either directly or through their toxic products; and (4) putrefactive fermentation within the alimentary canal with absorption of poisonous products.

While each of these causes may occasion albuminuria for a time without ascertainable renal lesion, sooner or later, with the continuance of the cause, there come the pathological changes which characterize true Bright's disease. These changes may be chiefly found in the tubules, creating degenerative changes in the epithelial element and constituting parenchymatous nephritis; or they may affect those parts in which connective tissue substance predominates the glomerular, interglomerular, and intertubular portions, giving rise to interstitial nephritis, or finally, both the epithelial element and the connective tissue element may be involved as in diffuse nephritis. Without going into the intimate cellular pathology, it is generally appreciated that these changes are distinctly not inflammatory in type, save in the single instance of the form known as acute exudative nephritis, where there is an intense determination of highly toxic blood to the renal capillaries. It is also a part of our general knowledge that as soon as these changes have become thoroughly established they are irreparable in a strict pathological sense. Possibly this may be less absolute in the form of nephritis which affects the epithelial element, since it has been urged by some that in parenchymatous nephritis an anatomical restoration to the normal is not impossible. There is, however, no evidence to show that there is ever a retrogression of the connective tissue overgrowth in interstitial nephritis. Physiologically speaking, these changes are anything but irreparable, since the renal function possesses compensatory powers against damage second only to those of the the heart. As Porter neatly puts it, the lesions of Bright's disease can never be cured to the eye of the pathologist and histologist, but to the physiologist and clinician the cure of the disease in a physiological sense, is both possible and probable. Physiological cure comes through the remissions which characterize this disease, and these may run the gamut from transitory abatement of symptoms to prolonged absence of all phenomena covering many years. The part which wise medical treatment may play in bringing about remission need not be dwelt upon. Is there a field here for surgical aid? Surely there is nothing pointing to the possibility of the knife accomplishing an anatomical cure of Bright's disease, until the chimerical proposition of replacing diseased kidneys with sound ones is brought about. In the meantime the question remains, Can surgery bring about physiological cure?

Let us look for a moment into the various theories which have served to explain the apparent successes after nephrotomy. Edebohls claimed that recovery was due to a new blood supply coming from the perinephric structures and penetrating the denuded sub-

stance of the kidney. This proposition was thoroughly exploded by the arguments of Tuffier and Claude, working independently, as well as by others, and by the observation of Reis, who examined six hundred denuded kidneys, to find in only one slight evidence of a new blood supply. Indeed, the source of a new blood supply would remain problematical even were it possible for the kidney to receive it, since, as was pointed out by the writer in an article on perinephric abscess, read before the Academy of Surgery, the decided inadequacy of perirenal circulation constitutes a potent cause for suppuration.

Under no circumstances, then, can any weight be attached to this neovascular theory.

Harrison's idea that recovery might come through the relief of tension cannot be dismissed quite as summarily, though here again there is faulty reasoning in some particulars. In the first place, his comparison of inflammation of the pancreas and of the testicle to the kidney in Bright's disease is unfair and unsound, both anatomically and pathologically. As I have just stated, Bright's disease is not in any sense an inflammatory process, and the renal capsule is not a material factor either directly or indirectly in the morbid changes which occur beneath it. Harrison seemed of the opinion that there was actual physical stress upon the capsule, but this is extremely doubtful. Several observers have stated that in many cases it not only was not tense, but on the contrary, presented a somewhat loose and wrinkled appearance. This may not always be the case, but it is assuming much to conclude that the removal of a relatively thin connective tissue covering, which certainly can be somewhat stretched, will affect to any extent an organ of the size and character of the kidney. Furthermore, it is now well known that after decapsulation, a new capsule is formed, which is thicker and less elastic than the original one. Carried to its logical conclusion, Harrison's thought seems almost as preposterous as to assume that splitting a glove covering a tightly clinched fist will make the fist relax. In Bright's disease it is the tight fist and not the glove which is the important factor.

From another point of view, namely, that the removal of the capsule may permit of the drainage of an edematously laden, blood-engorged, and, therefore, functionless or partially functionless area, the matter of tension presents an interesting phase which shall be presently mentioned. Pel and Jaboulay evolved the ingenious theory that the cures were brought about by a reaction of the sympathetic ganglia, due to the manipulation of the kidney during operation, and Sephonger, acting on this suggestion, devised an operation by which the kidney was secured by a flap of the quadrate muscle and covered by the internal oblique so as to obtain continuous massage. There are other interesting theories on this subject, such as the renorenal reflex explanation of the cures in

bilateral Bright's, where only one kidney was operated on, but time does not permit of their discussion.

To my mind the question resolves itself somewhat as follows: (1)There is no scientific justification for the assumption that surgery, or anything else, can cure Bright's disease once it is established. (2) The majority of the theories which have been advanced to warrant surgical interference have not been convincing, to say the least. If this were all, another chapter of valiant though vain endeavor should be considered closed, but that it is not all is shown by a constantly growing mass of clinical data which is deserving of the closest scrutiny and which strongly tends to show that the physiological cure of Bright's disease through remission may be brought about by operation. Despite an immediate mortality of about 30 per cent., and a mortality of 44 per cent., within a short period, it cannot be gainsaid that the results of the operative treatment have been other than hopeful when the desperately ill condition of many of these patients is taken into consideration. The reported cases, now running into many hundreds, show a striking number of recoveries, some of which can only be described as brilliant, and it is not surprising that nearly three-fourths of the surgeons who have expressed opinions are favorably disposed and satisfied with their results. It is interesting to note in this connection that these clinical results are supported by animal experimentation, at least to the extent that such experiments can throw light upon human conditions. Rovighi found with cantharides nephritis in rabbits that all recovered after operation, while 50 per cent. of the controls died; with diphtheria toxin nephritis 50 per cent. were saved by decapsulation, while 100 per cent. of the control animals died. Claude and Balthazard drew similar deductions from experiments on dogs.

What is the secret of these undoubted recoveries? Wherein lies the merit of surgical interference in Bright's disease? Have we another empirical measure of value like unto the operation of Spencer Wells for tubercular peritonitis, and, like it, not amenable to successful analysis? I hardly think so. I believe that nephrotomy in these cases does good and often saves life because it does, and does abruptly and thoroughly, certain things which are within the mental horizon of every medical student whenever he thinks of Bright's disease. The use of cups, dry and wet, over the kidneys is one of the oldest procedures in our armamentarium; venesection, and thereby the reduction of arterial hypertension, is an oft-neglected measure of such value as scarcely to be overestimated in the treatment of the critical phases of urinary suppression. I believe that cutting down upon the kidneys accomplishes all the purposes of cupping and of bloodletting, and does it better because it tends to relieve the disturbance at its focal point. Just as in intestinal obstruction the sympathetic nerve impulses create violent peristalsis to over-

come obstruction, so we may have in anuria and uremia intense local vasomotor efforts to overcome the renal block. Furthermore, the removal of the capsule seems wise. No man can say just what part is played in the case of suppression by the edema within the kidney itself, and decapsulation certainly offers an outlet. For this reason I believe with Harrison that these cases should always be drained. There may be other explanations for the value of surgical interference in restoring renal equilibrium based upon more precise knowledge of urinary physiology, but for the present these seem sufficient.

There can be no doubt from the published reports that it is in those cases where the factors of hypertension, local and general, and of edema are the predominant phenomena that the most successful results have been obtained, while the least satisfactory subjects for the knife have been those where the kidneys were caught in the death grip of interstitial change. Particularly apt has been the operation in saving life in the severe form of Bright's disease complicating and following the acute exanthemata, of which scarlatinal nephritis may be mentioned as a type. It is in these cases, where there is a rapidly diminishing quantity of bloody urine loaded with albumin, where deafness and blindness, convulsions, and coma occur, and where dissolution seems almost certain, that some of the brilliant recoveries have been recorded. The results in chronic parenchymatous and, to a minor extent, in diffuse nephritis have been less satisfactory, but, nevertheless, a judgment based on the experience of a large number of operators would tend to make us classify the operation as worth while. The average in these forms is brought up by the distinctly good results, broadly speaking, in young people. Even where physiological recovery has not been possible the operation has often secured abatement of the more distressing symptoms and prolongation of life. Finally, those cases in which the cardiovascular changes are marked are the least favorable of all. There seems to be but little excuse for surgical interference in interstitial nephritis.

Much must depend upon the care and good judgment with which cases are selected for operation. Already enough mistakes have been made in the theory and practice of this interesting field of curative endeavor. Bright's disease is and must remain a medical entity, and it is not until medical measures have been given a fair trial and have failed that we are justified in considering surgery. When that time comes these fairly well-defined principles may be borne in mind for guidance in the individual case: (1) That operation may be hopefully done in acute nephritis; (2) that young patients are the best subjects; (3) that there is sound reason for operating for anuria or uremia, occurring in chronic nephritis; (4) that operation may be resorted to as a last desperate chance in any form of nephritis.

With respect to the operation itself, I may say that when it was first proposed and practised, the choice of an anesthetic received considerable attention for obvious reasons, but since that time the development of spinal anesthesia has placed at our disposal a measure which is singularly well suited for the more critically ill of these cases, as I can attest from personal experience. Under all aseptic precautions the kidney area is invaded through a nearly vertical incision, extending from the inferior border of the twelfth rib to a little beyond the middle of the iliac crest. The latissimus dorsi fibers are split, the erector spinæ sheath is avoided, the quadratus lumborum is incised in its length, and the deep lumbar fascia opened. The perirenal fat is quickly pushed aside by blunt dissection until the bared convexity of the kidney is exposed. The capsule is split vertically, and by a gauze-covered finger is separated from the cortex and pushed in folds well in toward the pelvis. This can readily be done without delivering the kidney. The other kidney should then be similarly treated. The wounds are quickly closed with provision for drainage by tubing. The whole procedure should be done expeditiously, and a double decapsulation should only take a few minutes.

In the successful cases it has been found that the urine shows an increase in quantity and a decrease in morbid constituents within twenty-four or forty-eight hours, and in the majority of the recoveries the physiological cure is complete in from thirty to thirty-five days.

THE QUANTITATIVE DETERMINATION OF FUNCTIONAL RENAL SUFFICIENCY BY THE DUBOSCQ COLORIMETER; INDIGOCARMIN VERSUS PHENOLSULPHONEPHTHALEIN.[1]

A PRELIMINARY REPORT.

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(From the William Pepper Laboratory of Clinical Medicine.)

It is conceded that the most reliable individual kidney test is one dependent upon a quantitative metabolic study. By reason of the complicated conditions entailed, the requirement of particular physiologico-chemical knowledge, and the consumption of time demanded for the completion of the necessary observation, which

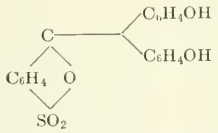
[1] Read before the College of Physicians of Philadelphia, February 1, 1911.

even then may not be conclusive as von Noorden has demonstrated, such a procedure is destined never to become popular. Indeed, the mere fact that every four or five years witnesses the announcement of a new method for determining the kidney function suffices to prove (1) that the old tests are inadequate or unsatisfactory, and (2) that it still remains the keen concern not only of the internist, but particularly of the surgeon, to find some test, whereby the health or disease of the kidney may conveniently be determined.

Various drugs and dyes have been utilized in countless attempts to solve this perplexing problem, in the subcutaneous employment of which attention has been directed to the time of onset of their elimination by the kidneys, to the constancy of reaction, and to the intensity, maximum, and duration of their excretion. Attempts to compute the quantitative elimination of these substances have never, until recently, been crowned with notable successes. Formerly, with methylene blue, in order to determine the amount of the dye excreted, the colored urine was measured and placed in a glass container. Precisely the same quantity of water was placed in another glass, and known quantities of methylene blue added until the two solutions became homogenous in coloration. The percentage of the aniline dye eliminated in the urine was then easily and approximately computed.

During the past year, Rowntree and Geraghty have called attention to the great advantages of phenolsulphonephthalein, a substance first described by Ira Remsen, for a functional renal test, placing especial emphasis upon the quantitative estimation of the percentage of the drug eliminated by the kidney during the first hour or two following its injection subcutaneously.

The structural formula of this phthalein may be represented as follows:



This substance is a bright red, crystalline powder, slightly soluble in water, but more so in alcohol; insoluble in ether; in dilute alkaline solution it is a purer red than phenolphthalein, being purple in strongly alkaline solution.

This phthalein has certain properties not possessed by phenolphthalein which recommends it highly in work on the physiology of the kidneys. It has a stronger avidity as an acid and is much more completely eliminated by the kidney than phenolphthalein. It may be administered by mouth and subcutaneously without ill effect. Employed more accurately by the latter method in doses of 6 mg. to the cubic centimeter, it is absolutely non-irritating, devoid of toxicity, and appears in the urine in normal individuals

in about ten minutes. It is also excreted in the bile, only to be reabsorbed, however, in the intestinal tract.

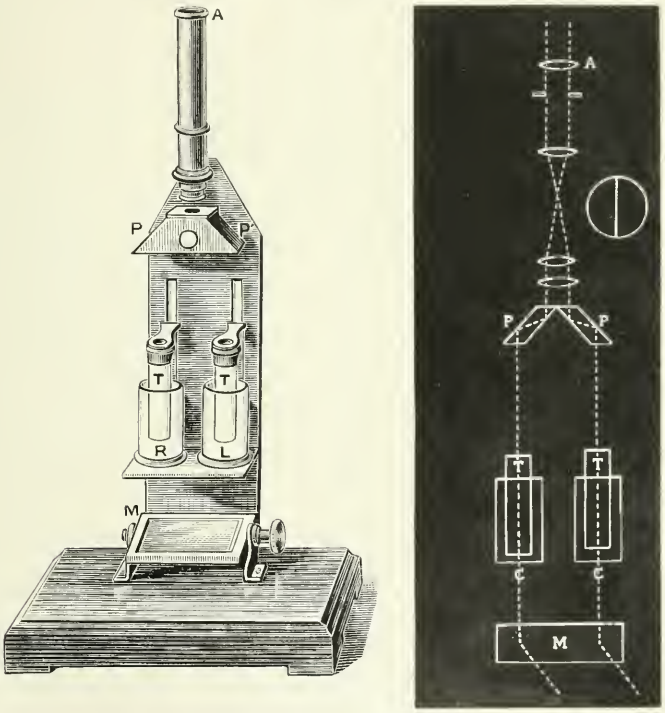
Phenolsulphonephthalein is unquestionably one of the very best substances at our command for purposes of functional renal diagnosis and prognosis. The test is very delicate, and, as is the case with phloridzin, it may prove to be oversensitive. Owing to the small quantity of the drug required for injection, which produces no pain or tenderness, it can be highly recommended to the internist for use in very sick and nervous patients, in whom it is desired to estimate the total renal function, but for unilateral diagnosis, the grave concern of the surgeon, it is extremely doubtful whether phenolsulphonephthalein can ever supplant indigocarmin.[2] The latter, although not eliminated so extensively by the kidney, has not yet been shown to be inferior to phenolsulphonephthalein as a quantitative functional test. It seems unfortunate that two such meritorious tests must be brought into comparison. It would be better, perhaps, if we were to differentiate the subjects suitable for the application of either, because in unilateral diagnosis indigo will suffice to meet the demand in cases impossible of ureteral catheterization, where the phthalein test must necessarily fail.

The technique of the phenolsulphonephthalein test is as follows: Fifteen minutes to half an hour before administering the test the patient is requested to drink two glasses of water to insure free renal activity. One c.c. containing 6 mg. of the phthalein is injected subcutaneously.[3] If it is desired simply to learn the total kidney sufficiency, as may be the case in the various forms of nephritis, or the extent of renal drainage due to vis a tergo pressure, atrophy of the parenchyma of the organs, etc., because of obstruction in the lower urinary tract, as by prostatic enlargement, etc., a catheter is introduced into the bladder and the onset of the excretion of the phthalein noted by the beautiful amethyst-red produced when it comes in contact with the drop or two of 25 per cent. sodium hydroxide placed in the bottom of the receptacle used for collection. The quantities of urine for the first and second, or possibly third, hours are then collected. Instead of the procedure by catheterization, at first continuously and then hourly, the patient may be requested to void voluntarily every five minutes until the onset is observed, and then at hourly intervals. Such a procedure is simplicity itself, but not more so than the indigocarmin technique. On the contrary, if it be desired to determine the functional activity of the individual kidneys separately, an act is demanded which may be, and not

[2] For description and technique for employment of this dye in functional kidney diagnosis, see author's articles, "Chromocystoscopy in Functional Renal Diagnosis, Based upon the Employment of Indigocarmin," Surg., Gyn., and Obstet., April, 1909, or Penna. Med. Jour., September, 1909; "Uber die Chromoureteroskopie in der funktionellen Nierendiagnostik," Zeit. f. Urologie, April, 1911; or "The Value of Chromoureteroscopy in Functional Kidney Diagnosis," Surg., Gyn., and Obstet., May, 1911.

[3] This substance is prepared by Hynson, Westcott & Co., Baltimore, Md.

infrequently is, impossible, namely, catheterization of one or both ureters, in order to convey the phthaleinized acid urine externally to an alkaline medium, so as to study the color reaction. With indigocarmin, catheterization of the ureters is rarely necessary, since the onset of the indigo elimination can be readily seen through the cystoscope as the blue jets of urine are ejected from the ureteral orifices into the bladder. Indeed, from an analysis of over one hundred cases subjected to the indigo test, the time of onset runs a close parallel to the quantity eliminated, and judging alone from the time and character of the elimination, in no instance has a false prognosis relative to renal sufficiency or insufficiency been made.



Duboscq colorimeter.

It has been alleged against indigocarmin that it does not lend itself well to colorimetric determinations. It is claimed that the urinary constituents cause a decomposition of the dye. With this statement I cannot agree, and believe that indigo is as efficient as the phthalein for colorimetric readings.

It is indisputable that for certain kidney conditions quantitative determinations are most valuable, whether the substance employed be indigocarmin, phenolsulphonephthalein or what not. During the past year or two Oppenheimer and Rowntree and Geraghty have

employed the Duboscq colorimeter with gratifying success for the estimation of renal activity, and the last two in particular are very high in their praise of the instrument.

As shown in the figures, the Duboscq colorimeter consists of two glass cylinders, cut with parallel plane surfaces placed on arms capable of vertical movement by the manipulation of set screws on the posterior surface of the instrument. These crystals may be raised and lowered in glass reservoirs containing solutions, the comparative colors of which are to be determined. In one reservoir, R, is placed the standardized solution; in the other, L, the solution to be tested. The mirror M is adjusted so as to reflect light through the perforated stage, S, into the reservoirs supported by the same, thence to the glass parallelopipeds P and P', and so through the telescope to the ocular A. By manipulation of the set screws the crystals are elevated or lowered until a homogeneous coloration appears at the ocular. Scales, with Vernier attachments, invisible in the figures, furnish the readings from which the percentage of color in the solution to be tested can be computed.

In the performance of the colorimetric test, $\frac{1}{2}$ c.c., containing 3 mg. of phenolsulphonephthalein[4] is placed in a flask and diluted up to 1000 c.c., adding one drop of 25 per cent. sodium hydroxide to elicit the amethystine coloration. This can be preserved indefinitely for future determinations. The reservoir R is then about one-half filled with this control solution and the plunger lowered until the index on the scale reads 20. This reading is arbitrary, as any other may do. Within a few minutes following the subcutaneous injection of the patient with 1 c.c. or 6 mg. of the phthalein, it begins to be eliminated in the urine, occurring normally in the acid state as an orange yellow. This may be collected by voluntary urinations, by urethral catheterization, or by ureteral catheters if the work of the kidneys individually is desired. The onset of elimination is determined by collecting the urine in the presence of a drop or two of the sodium hydrate solution, noting the occurrence of the pinkish color. Quantitatively, the amounts of the first and second hours are collected separately. Each amount is rendered definitely alkaline by the addition of sodium hydrate and is diluted up to 1000 c.c. A quantity of this is filtered and placed in the reservoir L. The left hand set-screw is then manipulated until a similar coloration is observed on both sides, and the reading taken. If, for example, the reading on the left is found to be 40, and, as previously stated, the control reads 20, it is obvious that the solution to be tested is only half the concentration of the control, which may

[4] If indigocarmin is used, 5 c.c. of a 0.4 per cent. solution is placed in the flask for the preparation of the control solution. It will be noted that only a fractional part, in the case of the phthalein one-half and with indigo one-fourth, of the amount administered to the patient is employed in the control. This is done because the solutions in these dilutions lend themselves more favorably to colorimetric readings.

be graphically represented as follows: $\frac{2}{4}\frac{0}{0} \times 100 = 50$ per cent. Inasmuch as the control is made up of but one-half in the case of phenolsulphonephthalein, and only one-quarter in the case of indigocarmin, of the amount injected into the patient, it is necessary in the former instance to divide the result by two and in the latter by four in order to determine the actual percentage eliminated of the amount injected into the patient.

The Dubosceq colorimeter is an ideal instrument for quantitative colorimetric determinations, not only by virtue of the simplicity of its construction, but also because of the accuracy of results obtained by its use. A review of Table I will demonstrate the close parallelism existing between the findings with this instrument as compared with known solutions of indigo and phthalein.

TABLE I.—Solutions in distilled water.

No.	Known quantity of indigocarmin.	Amount estimated.	Known quantity of phenolsulphonephthalein.	Amount estimated.
1	0.0014 gram	0.0013 gram	0.0027 gram	0.0028 gram
2	0.0039 "	0.0039 "	0.0023 "	0.0024 "
3	0.0029 "	0.0028 "	0.0037 "	0.0037 "
4	0.0056 "	0.0057 "	0.0042 "	0.0043 "
5	0.0053 "	0.0052 "	0.0055 "	0.0055 "
6	0.0071 "	0.0071 "	0.0074 "	0.0074 "
7	0.0065 "	0.0065 "	0.0089 "	0.0088 "
8	0.0087 "	0.0086 "	0.0087 "	0.0087 "
9	0.0078 "	0.0078 "	0.0095 "	0.0095 "
10	0.0093 "	0.0094 "	0.0098 "	0.0098 "

That quantitative colorimetric determinations of indigocarmin and phenolsulphonephthalein in functional kidney diagnosis are of great value is undisputed. Whether or not the quantitative estimation will in time supersede in value the onset of elimination is a mooted question and to my mind a very doubtful one, save for the determination of the total renal function particularly for the purposes of the internist. There can be little doubt that in certain conditions, as nephritis, and especially in prostatic enlargement, where, as a rule, the kidneys are more or less damaged by a vis a tergo pressure from retained urine, the colorimetric determinations are of exceptional value, and I confidently believe that every surgeon contemplating prostatectomy will not only decrease his mortality, but will also avoid debasing the profession of medicine, by refusing to operate in such cases when the total output for the first hour of indigo and phthalein falls below 10 and 20 per cent. respectively. I have long since been convinced that an onset of the elimination of indigo after twenty minutes bespeaks renal insufficiency and contraindicates operative interference. Again, it must be borne in mind that even though the quantitative elimination is found to be below the figures above stated, operation may be considered, provided the elimination during repeated determinations remains constant, evidencing no tendency to fall, thereby establishing a stable

kidney activity. On the contrary, an operation undertaken in the presence of a steadily decreasing functional capacity, as measured most accurately and satisfactorlly by colorimetric determinations, is little short of criminal, as the patient will invariably die.

An important field which should be studied, relative to the quantitative elimination of indigo or phthalein, is that of all operative cases. It is quite possible that by an analysis of several hundred cases thus tested by these substances before operation, data might be derived that would in the future lower the general surgical mortality.

The problem that I hope to solve eventually—as I do not think the results of the cases analyzed to date sufficiently conclusive—is the determination of the relative merits of indigocarmin and phenolsulphonephthalein. In order to accomplish this I have undertaken comparative studies of the action of both substances on a series of dogs and patients. It was at first attempted to study the onset of elimination of both substances from the ureteral orifices into the bladder of large female dogs by cystoscopy. The procedure was difficult, owing to the fact that the etherized dog seemed able to retain very little fluid in the bladder in the presence of the cystoscope. It was also very evident that the anesthetic (ether) markedly diminished the excretion of urine and, in one case at least, produced anuria. In the dogs subjected to indigocarmin, the fluid used for distending the bladder was water; in those injected with phenolsulphonephthalein, the fluid employed was 25 per cent. sodium hydrate. In no case was indigo or phthalein eliminated from the ureteral orifices for forty-five minutes. At the termination of that period the dogs were allowed to revive from the anesthetic. The two dogs injected with indigo immediately voided a faintly blue-colored urine; one dog having received phthalein voided at the end of an hour, the urine demonstrating the presence of that drug, the fourth dog refused to urinate. The results are tabulated below:

TABLE II.—Dogs Cystoscoped.

No.	Substances used in tests. Indigo.	Phthalein.	Appearance of drug by cystoscopy, under ether.	Onset of secretion subsequently.
1	20 c.c. of 0.4 %		0	45 minutes.
2	20 c.c. of 0.4%		0	45 minutes.
3		1 c.c. =6 mg.	0	60 minutes.
4		1 c.c. =6 mg.	0	

Owing to the poor success of the first attempt, it was decided to perform ureterotomies under ether in the second series, catheterizing the ureters and collecting the respective urines, both for onset of elimination and quantitative study. The results are noted in Table III.

TABLE III.—Dogs Operated Upon.

No.	Substances used in tests.		Onset in minutes.		Quantitive determinations.						
					First hour.		Second hour.		Third hour.		
	Indigo.	Phthalein.	Right ureter.	Left ureter.	Right ureter.	Left ureter.	Right ureter.	Left ureter.	Right ureter.	Left ureter.	Total.
1	40 c.c. of 0.4%		5	5	1.63%	1.03%	1.37%	0.51%	1.48%	0.64%	6.66%
2	40 c.c. of 0.4%		45	45	.....	.....	trace	0.29%	.....	.....	0.29%
3	.....	2 c.c. = 12 mg.	0	0	0	0	0	0	.....	..	Nil
4	.....	2 c.c. = 12 mg.	15	15	1.35%	2.41%	trace	1.32%	0	0.35%	5.43%

Judging from the few dogs thus far utilized, there would seem to be slight preference in favor of indigocarmin. By multiplying the number of experiments with dogs, I hope eventually to throw some light on this important problem, although it is not improbable that the human subject will suffice to settle the dispute.

In Table IV are tabulated a number of cases, normal and diseased, that have been subjected to the indigocarmin and phenolsulphonephthalein tests. In a few instances, comparative applications of both methods for as many as four hours have been made.

It will be observed from a review of the tabulated cases, although too few in number for absolute conclusion, that the onset of elimination of both indigo and phthalein runs a close parallelism with the quantitative output; that as substances for quantitative determination in the estimation of renal sufficiency, they are essentially equal in value; that both substances are largely eliminated during the first two hours after injection; that the percentage output of indigo is approximately about one-half that of phthalein, which fact, however, is of no moment in drawing conclusions; that in normal ambulatory cases the onset occurs in about ten minutes, while the total output exceeds 60 per cent. of the amount injected; that in contradistinction to the ambulatory cases, the bedridden patients, even though possessing supposedly normal kidneys, exerete less than one-half of the amount eliminated by the cases at liberty to move about, and, finally, that the output of indigo occurs slightly earlier and continues no longer than the phthalein.

CONCLUSIONS. 1. Quantitative colorimetric determinations of indigocarmin and phenolsulphonephthalein are of very great value in the estimation of the total renal function, particularly in such conditions as nephritis and damaged kidneys, incident to prostatic enlargement, etc., causing poor drainage and resulting in vis a tergo pressure. These substances routinely employed by the surgeon as indicators for or against surgical intervention, particularly in contemplated prostatectomies, but likewise in other fields of surgery, will aid materially in the reduction of operative mortality.

Table IV.—Quantitative Colorimetric Tests on Human Beings.

Normal Cases.

Name.	Diagnosis.	Indigocarmin. Amount injected.	Onset. R	L	Quantity eliminated. 1 hr.	2 hrs.	3 hrs.	4 hrs.	Total.	Phenolsulphonephthalein. Amount injected.	Onset. R	L	Quantity eliminated. 1 hr.	2 hrs.	3 hrs.	4 hrs.	Total.	Urinalysis and Remarks.
L. S.	Normal (ambulatory)	8 mg.	Before 10 min.		11.84%	4.86%	1.75%	0.91%	19.36%	6 mg.	Before 10 min.		37.59%	23.69%	9.62%	..	70.9 %	Negative.
I. G. C.	Normal (ambulatory)	8 mg.	Before 9 min.		10.86%	8.44%	2.06%	1.01%	22.37%	6 mg.	Before 9 min.		58.47%	6.28%	3.62%	1.4%	69.77%	Negative.
S.	Normal (ambulatory)									6 mg.	Before 15 min.		33.44%	18.66%	5.62%	4.32%	62.04%	Negative.
B. A. T.	Normal (ambulatory)	8 mg.	5 min.		7.53%	?	2.56%	1.44%	?	6 mg.	Before 9 min.		30.12%	18.38%	13.58%	3.76%	65.84%	Negative.

Abnormal Cases.

R. C.	Nephrolithiasis (Rt.) (bedridden)	8 mg.	10 min.	7 min.	3.35%	5.47%	1.35%	0.51%	10.68%	6 mg.	18 min.		11.00%	6.95%	3.22%	1.89%	23.06%	*Urine:* negative save for few erythrocytes. Calculus 1 cm. in diameter removed.
W. E.	Myocarditis (bedridden)	8 mg.	9½ min.	9½ min.	10.82%	2.07%			12.89%	6 mg.	?		5.91%	21.36%			27.27%	*Urine:* Acid, 1012, faint trace of albumin, hyaline and light granular casts, cylindroids, mucus. *Blood pressure* {Sys. =185 Dias. =125
M. K.	Nephritis, interstitial, chronic (bedridden)	8 mg.	13 min. feeble	0 in 30 min.	0.90%	0.86%	..	..	1.76%									*Urine:* Acid, 1009, cloud of albumin, hyaline and light granular casts, cylindroids, leukocytes. *Blood pressure* {Sys. =220 Dias. =125
J. S.	Nephritis; tuberculosis, pulmon. (bedridden)	8 mg.	9 min.	9 min.	4.03%	6.49%			10.52%	6 mg.	No e	liminati	on for a	period	of two	hours.		*Urine:* Acid, 1019, cloud of albumin, many hyaline and light granular casts, few erythrocytes, mucus. *Blood pressure* {Sys. = 125 Dias. 80
C. O.	Prostatic hypertrophy; cardio-renal disease (bedridden)	8 mg.	15 min.	15 min.	6.25%	1.56%			7.81%	6 mg.	20 min.		7.22%	9.61%			16.83%	*Urine*: Acid, 1015, faint trace of albumin, few hyaline and granular casts, few red blood cells and white blood cells. *Blood pressure* {Sys. =165 Dias. =105
H. R.	Nephritis, hemorrhagic? (bedridden)	8 mg.	11 min.	12½ min.	?	?			2.04%									*Ureteral Catheterized Specimens*: Acid, 1015, heavy cloud of albumin, leukocytes and pus cells, erythrocytes, bacteria, no casts.

N. A.	Diabetes mellitus (bedridden)	6 mg.	15 min.	2.61%	23.07%	trace		25.68%	Sugar=6.25%.
J. McD.	Endocarditis (bedridden)	6 mg.	Earlier than40, not at 20 min.	? 3.1 %	? 9.04%	? 10.12%		13.87% 22.26%	*Urine:* Acid, 1028, large amount of albumin, pus, hyaline and granular casts, cylindroids. Lost cardiac compensation.
B. O.	Nephritis, parenchymatous, chronic (bedridden)	6 mg.	12 min	10.80%	9.35%	2.8 %		22.95%	*Urine:* Acid, 1021, albumin =9 pro mille (Esbach), many hyaline, light and dark granular casts, colloid casts, many white blood cells. *Blood pressure* {Sys. =140 Dias. =120
D. W.	Nephritis, interstitial, chronic (bedridden)	6 mg.		1.61% 2.77%	9.34% 11.95%	5.26% 18.56%		16 21% 33.28%	*Urine:* Alkaline, 1018, trace of albumin, few hyaline and granular casts, few erythrocytes. *Blood pressure* {Sys. =235 Dias. =150
R. C.	Fracture, compound; amputation of leg; (bedridden)	6 mg.	?	3.11%	1.28%	0		4.39%	*Urine:* Cloud of albumin, few cylindroids, leukocytes in excess.
J. J.	Lymphadenectomy (bedridden)	6 mg.	11 min.	22.83%	5.18%	trace		28.01%	*Urine:* Acid, 1023, faint trace of albumin, hyaline and light granular casts, many cylindroids, mucus, excess of leukocytes.
H. S.	Tuberculosis, hip (bedridden)	6 mg.	59 min.	21.36%	?	1.06%		22.42%	*Urine:* Alkaline, 1008, faint trace of albumin, few polynuclear granular casts, few cylindroids, leukocytes, erythrocytes.
G. P.	Varicocele, postoperative (bedridden)	6 mg.	30 min.	14.04%	10.57%	1.01%		25.62%	*Urine:* Alkaline, 1022, faint trace of albumin, normal leukocytes, epithelium.
L. B	Tuberculosis, os calcis. (bedridden)	6 mg.	20 min.	30.03%	1.59%	trace		31.62%	*Urine:* Acid, 1021, few hyaline casts, cylindroids, leukocytes in excess, mucus.
F. W.	Wound, gunshot, spine; monoplegia (bedridden)	6 mg.	12 min.	12.72%	1.12%			13.84%	*Urine:* Alkaline, 1026, faint trace of albumin, mucus.
H. J.	Tuberculosis, spine; psoas abscesses; amyloid kidneys? (bedridden)	6 mg.	29 min.	trace	0			trace	*Urine:* Acid, 1017, trace of albumin, hyaline, dark and light granular casts, normal leukocytes, mucus.

2. Although each substance has its particular advantages and indications as a test, indigocarmin, at least for the purposes of the surgeon, especially in the diagnosis and prognosis of unilateral renal disease, seems just as useful and possibly more practical than the new drug phenolsulphonephthalein.

3. Phenolsulphonephthalein in many respects is an ideal substance for employment in studying the pathology and physiology of the kidney. It may possibly be more sensitive than indigocarmin, in fact, may prove to be too delicate. On the other hand, the technique of the test is extremely simple and may be employed painlessly. Preference should be extended to this drug over indigocarmin whenever it is desirable to learn the total or combined efficiency of both kidneys.

In conclusion, I desire to express my grateful appreciation to Drs. Edsall, Frazier, Riesman, and T. T. Thomas for permitting me to use material that made it possible to conduct, in part, these studies.

ACTINOMYCOSIS IN NORWAY: STUDIES IN THE ETIOLOGY, MODES OF INFECTION, AND TREATMENT.

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Actinomycosis is far from being a rare disease. Cases have now been studied in nearly every country. In America, Hodenpyl[1] published studies on this disease in 1890, and 1899 Ruhräh[2] reported a large series of cases observed in America.

The first case of actinomycosis was reported in Norway as early as 1887, and since that time scattered cases have occurred, but up to this time a collective report has not been brought forth. During the last fifteen to twenty years the Institute for Pathological Anatomy has been investigating a large series of instances of actinomycosis. The material was obtained partly from autopsy and partly from pathological material sent to us by the practicing physicians in various parts of Norway.

[1] Hodenpyl, 1890, Actinomycosis of the Lungs, N. Y. Med. Record, 1890, and Erving, W., Actinomycosis Hominis in America, with Report of Six Cases. Johns Hopkins Hospital Bull., 1892.

[2] Actinomycosis in Man, Annals of Surgery, October to December, 1891.

Etiology. Our series includes 87 cases, and the lesions were distributed as follows: 45 per cent. occurred on the neck and face (all cured); 23 per cent. in the thorax (all dead); 30 per cent. in the abdomen (19 dead, 5 cured); 3 per cent. on the skin (1 dead, 1 cured).

We have reasons to believe that this represents approximately the relative frequency on various parts of the body: 56 occurred in men, 27 in women, and in 7 the sex was not given. The relative age is given: 2 occurred in the first decade (boys); 12 occurred in the second decade (10 men, 2 women); 26 occurred in the third decade (17 men, 9 women); 16 occurred in the fourth decade (10 men, 6 women); 13 occurred in the fifth decade (8 men, 5 women); 7 occurred in the sixth decade (4 men, 3 women); 3 occurred in the eighth decade (3 men).

Among the 39 cervico-facial cases, in 15 the lesions were located on the cheek especially on the maxilla, the forehead, and the parotid region; in 20 they were on the mandibular or on the submental region and in 3 they were located farther down the neck, and one tumor was on the tongue.

The infection atrium was in every instance the mucous membrane of the oral cavity, and often the part covering the gums. There was no evidence of the fungi having entered by carious teeth as is supposed to take place by Lord.

All the 39 cases recovered.

In our thoracic group the primary lesion was always in the lungs, and, as a rule, in the lower lobes. The disease simulated an atypical bronchopneumonia or pulmonary tuberculosis, with fever, dyspnea, cough, and a rusty tenacious sputum, which, as a rule, contained the characteristic sulphur granules. Everyone of these terminated fatally.

The average duration was one to one and one-half years. One lived on for eight years.

The primary lesion of the abdominal cases was some part of the alimentary tract, most often the vermiform appendix. There were no primary lesions in the rectum, bladder, or genital organs, although gravitation abscesses did extend into these organs. The disease occurred as localized abscesses most often in the ileo-cecal region. These spread both extra- and intra-peritoneally. Liver abscesses were frequently found. The average duration of the fatal cases was one to two years.

In the two patients where the disease was primary in the skin, one had a localized abscess on the arm which soon healed. The other had a phlegmonous infection of the leg, that originated from an ulcer that started during the harvest. This man's leg was amputated, but he died.

Pathological Anatomy. The lesions occur in the form of a chronic suppurative inflammation with marked infiltration and a

relatively small amount of a thick tenacious pus. The characteristic feature of actinomycotic inflammation is its advance through all tissues or organs with the development of fistulous tracts. These lead into abscesses containing the typical pus. The internal organs are attacked from the periphery, and large abscesses always result. In the later stages general infection occurs through the blood with the formation of abscesses in the lungs, liver, kidneys, etc. It does not spread through the lymphatics except near the very end of the disease. In this way actinomycosis differs from other chronic inflammations, such as tuberculosis or glanders. Microscopically nothing striking is seen. Marked hemorrhagic infiltration is often observed and the giant cells are abundant.

The striking and perhaps pathognomic thing in actinomycotic inflammation is the presence of the sulphur granules. These are formed from mycelia and often contain the so-called clubs. They vary in size, color, and consistency, and there are rather marked differences between those found in man and cattle. In man the granules are usually pin-head sized; they are round or oval; of a grayish-white or yellowish color and usually of a soft consistency; rarely are they infiltrated with calcium. The color may be green or even brownish-black. With low magnification they appear as light yellow rosettes, consisting of a central mass of mycelia which radiate toward the periphery forming radial stripes (Fig. 1). The granules are surrounded by a dense zone of leukocytes. With the high power one may at times notice club formation at the ends. If they are present, the virulence of the fungus is low. Soft small granules are always found in rapidly growing lesions. In actinomycosis bovis the granules are larger, more distinct, and have a decided yellow color. They show club formation and are often partially calcified (Figs. 2, 3, and 4). They consist then of degenerated threads having very scant power of growth on media. Spores have never been seen.

Remembering then that the characteristic things in actinomycosis are a chronic inflammation advancing through all tissues, producing fistulous tracts from which ooze a thick tenacious pus containing sulphur granules and that generalized infection occurs only through the blood stream we pass to a study of the cultural characteristics of the fungus.

Cultural Characteristics. Much work has been done by many investigators in different countries for the purpose of determining the typical growth of the pathogenic fungus or fungi, and greatly varying results have been obtained; thus Boström and a large number of others have isolated a fungus growing in aërobic cultures producing aerial hyphæ, and showing true branching; it also colors the media yellow. This type has been identified with the actinomyces occurring in nature. Then another group of workers

among which are Wolff, Israel, J. H. Wright,[3] and Shiata,[4] have isolated an anaërobic fungus from actinomycotic lesions in men. Besides these two, a number of streptothrix more or less similar to the above have been cultivated from chronic inflammations where no sulphur granules occurred.

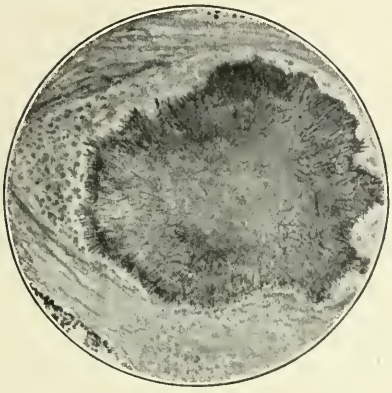

Fig. 1.—Human actinomycosis. Distinct radiation but indistinct bulbs. × 300.

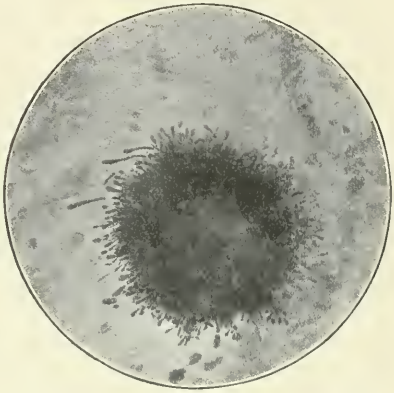

Fig. 2.—Bovine actinomycosis. Granules with marked calcification. × 300.

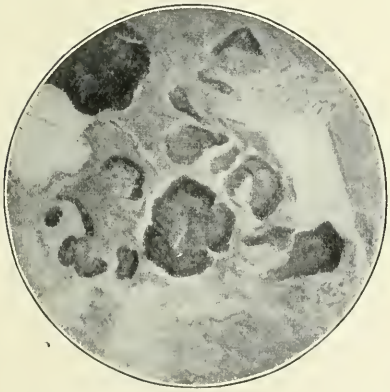

Fig. 3.—Bovine actinomycosis. × 80.

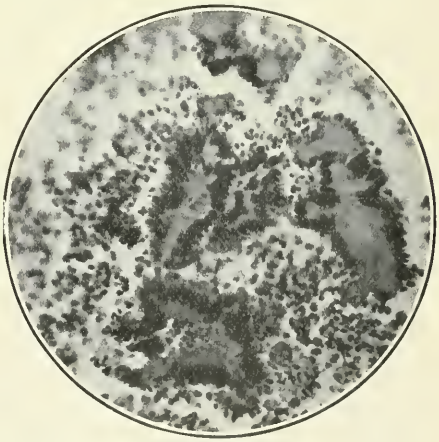

Fig. 4.—Bovine actinomycosis. Granules with marked calcification in the periphery; centre homogeneous without definite thread formation.

Because of this uncertainty as to which type was the real cause of the actinomycotic inflammation we decided to carry on a series of experiments to determine the exciting factors in our cases, and a brief statement of our work follows.

During the last year we made cultures of all the cases secured,

[3] Biology of Microörganism of Actinomycosis, Pub. of the Mass. Gen. Hosp., 1905, vol. i, No. 1.
[4] Beiträg zur Kenntniss die menschlichen Actinomycosis, Deut. Ztschr. f. Chir., 1909, Band ci.

but obtained pure cultures from only about half of them. Growth was more easily obtained from the small soft grayish granules. Pure cultures were obtained from 10 cases and seventeen strains were isolated, partly by making cultures at different times from the same lesion, and partly by inoculating media from pus, urine, or sputum from the same patient. If we add to our results the results of investigations carried on at the Pathological Institute where pure cultures were obtained from 5 cases by Dr. Kjerschow and 5 by Professor Harbitz, it makes a total of 20 cases with twenty-seven strains. Eleven of these were from the cervical facial types, three from the lungs, and four from the intestines.

Method. Pure cultures were obtained by putting the granules on slant agar and leaving them in daylight and at room temperature for three days. Then subcultures were made on the ordinary aërobic and anaërobic media and the cultures kept at 37° C. By this method we grew an anaërobic type, agreeing in all essentials with the one isolated by J. H. Wright. In agar stabs, the anaërobic growth was visible on the third day, and by the ninth colonies the size of a pinhead appeared as a dense zone about one centimeter from the surface. Each colony was similar in structure to a sulphur granule. Practically no growth appeared on aërobic agar slants, but it grew luxuriantly under anaërobic condition. Aerial hyphæ were never observed. In bouillon cultures grew aërobically but especially well anaërobically. Milk was not coagulated. Growth did not occur on glycerin serum, potato, gelatine, peptone broth, or raw eggs.

In order to keep the cultures alive it was necessary to transplant them about every tenth day. However, we did obtain a culture from a one hundred and forty-five day old granule. No odor, gas, or color was produced. The fungus grew very well in agar to which 1 to 2 per cent. of potassium iodide had been added. The fungus showed absolutely no tendency toward adopting an aërobic habitat, though we kept one strain through twenty generations. In old cultures the threads were branched and difficult to stain.

With the anaërobic fungus thus obtained we now carried out animal inoculations; the animals used were rabbits and guinea-pigs. Inoculations were made intraperitoneally, intrapleurally, and subcutaneously, first with sulphur granules and only once did an abscess develop in the pus of which were found granules, but this was probably not due to a real growth of the fungi. Inoculations from cultures, too, were negative. We also grew a pure culture of an anaërobic fungus, from an actinomycotic abscess in a cow, and made animal inoculations, but again failed to obtain results.

From the above we conclude that the anaërobic fungus isolated by us from many cases of actinomycosis hominis is the exciting cause of the disease in man, in at least the large majority of cases, and this conclusion is greatly strengthened by the fact that our

results are practically identical with the ones obtained by Wolff, Israel, J. H. Wright, and Shiata. It is also probable that the organism producing the disease in cattle is identical with that in man, but further work must be carried on to substantiate this.

We also examined a number of other strains supposed to be the cause of actinomycosis, but they were all aërobic and differing widely from ours. Having thus determined that the anaërobic fungus was the true cause of actinomycosis, it was left to find out, if possible, just what relation it has to the actinomyces found in nature; for botanists have obtained pure cultures and thoroughly studied many different varieties. Since we lacked time to carry on experiments to determine this relation we persuaded an able botanist, Mr. Hagen, to investigate this matter. Mr. Hagen obtained pure cultures of three strains from the air, but they were all aërobic fungi, and so were the two pure strains he secured from straw. He also grew three pure cultures from barley and oats; everyone of these had marked aërobic tendencies as had also a pure culture from manure. It might be added here that Mr. Hagen made an inoculation from an actinomycotic lesion and recovered a pure culture of the anaërobic fungus we had isolated. From his work, Mr. Hagen concluded that actinomyces hominis occurs rarely if at all in nature and if it does occur, it must exist under certain conditions only. His experiments, however, are too few from which to draw definite conclusions.

If the pathogenic fungus does not occur in nature, how, then, is the disease transmitted? Here it must be admitted that the mode of transmission is by no means clear. We have already shown that the fungus gains foothold through the lungs, the mucous membrane of the mouth or that of the intestines, but whence does it come? Is it found in the organism or on the outside and through what medium does it enter tissues? These are questions yet to be solved.

Up to this time it has been taken for granted that the fungus producing the disease in men is identical with the exciting cause of actinomycosis bovis. This has not been definitely proved. Actinomycosis hominis has also been thought to occur more frequently among country people associated with cattle. This we have found not to be the case. It is as common in cities as among farmers. Infection to man from cattle is, therefore, not probable, and since the disease always occurs as isolated cases in far separated localities, we are not justified in assuming that direct infection from man to man occurs.

It has been supposed that the pathogenic fungi are carried to the tissues by straw, slivers, and other parts of plants. This hypothesis has been based on two things: (1) That the natural and the pathogenic fungi are identical. This we have shown to be erroneous. (2) That straws, slivers, etc., have often been found in actinomycotic

abscesses. Pieces of plants are found especially frequently in the mouth lesions of cattle (Fig. 5). One must bear in mind, however,

FIG. 5.—Actinomycelial granule lying beside an awn in actinomycotic bovine granulation tissue. × 80.

FIG. 6.—Cross-section of awn with actinomycosis in the central canal and growing outward. From bovine tongue. × 300.

that these might have entered the abscesses secondarily. But straws have also been found in cervico-facial abscesses in man. To be sure, such findings are much rarer in man than in cattle, never-

theless, pieces of plants do occur. It is of special interest to note that abscesses always developed after a latent period varying from months to years after the entrance of such *corpora aliena*. Abscesses have also occurred after puncture of the mucous membrane with wooden splints, fishbones, pieces of glass and in one of our patients, after an abrasion on the leg. The finding of mycelial threads in or around these objects has served to strengthen the idea that they are the real carriers of the infection (Fig. 6). There is then some definite evidence showing that straws, splinters, etc., do play an indirect role in the transmission of actinomycosis, but there is certainly nothing to prove that the disease is directly transmitted by them.

Since the fungus is not carried directly from the outer world into the animal tissues the idea that it lives as a saprophyte on the mucous membrane and enters the tissue to produce lesions naturally suggested itself. It must also be remembered that infection does not take place by the granules, since they are a pathological product produced after the fungus has gained foothold. Infection then must occur either through threads or by some unknown form. Two possibilities confront us—(1) either the fungus lives as a saprophyte on plants to enter man by chance and then to go on living a saprophytic existence until a *locus minoris resistentiæ* is offered, when it becomes at once pathogenic, or (2), as J. H. Wright has suggested, the fungus is pathogenic from the start and lives on the mucous membrane ready to enter the tissues when aided by foreign bodies. Where the fungus might originate, Wright does not suggest. Both the above hypotheses depend on the demonstration of the fungus on the mucous membrane. What is known concerning this?

Mycelia, thought to be actinomycotic, have been found by Miodowski in the tonsils and the ductus lacrimalis. But much weight can not be placed on these findings since cultures were never made.

But we obtained from the tear sac of a student who had been suffering for over a year from a chronic dacryocystitis, a granule consisting of mycelia, and closely simulating the sulphur granules of actinomycosis. From this granule inoculations were made and a pure culture of an anaërobic fungus was grown. The cultural characteristics of this strain were very much like the ones of the fungus grown from actinomycotic lesions. Whether this fungus was the cause of the dacryocystitis or not is hard to determine, but the finding of it does indicate that the fungi may be present on the mucous membrane.

Finally, a word about the existence of actinomyces in carious teeth. Professor Partsch[5] and his pupils have reported the findings

[5] Jaehn, Die Aktinomycosis des Mundes, Deut. Monatschr. f. Zahnheilk., Heft 1 to 3, 1909.

of numerous sulphur granules in decayed teeth and in the pus of perialveolar abscesses. These again simulated those producing actinomycosis only morphologically. No cultures were made. J. H. Wright and Lord[6] carried on some very interesting experiments along this line. They obtained from carious teeth mycelial threads like those of the pathogenic fungus. These they inoculated into guinea-pigs and observed the formation of abscesses containing typical sulphur granules. Unfortunately they did not recover the fungus in pure cultures. We also inoculated material from carious teeth taken both from people who were well and from patients suffering from actinomycosis, but our results were invariably negative.

It is plain from the above that nothing very definite is known about the habitat of the actinomyces hominis prior to its attack on the tissues. Further investigations along this line are called for.

Treatment. In conclusion, a few words about the treatment of this disease. Up to the present time it has consisted of local surgical treatment and internal medication. Locally the lesions is removed entirely when practicable, but this can seldom be done, hence surgeons often resort to curettage or simple incision. Local injections of potassium iodide have been tried. Potassium iodide has also been given internally and good results claimed. But since we have shown that the fungus grows luxuriantly in 1 to 2 per cent. potassium iodide, its curative value is doubtful. The behavior of the disease is so extremely varied that the effect of any treatment is hard to judge.

The fact that a great variety of medicines have been recommended in the treatment of actinomycosis plainly shows the need of a specific treatment. But, in order to obtain any kind of serum therapy, great obstacles must be overcome: (1) The organism is hard to grow, their pathogenicity for lower animals is slight, to say the least. (2) The production of toxins is scant. (3) It is next to impossible to use the mycelia in agglutination tests.

French investigators have developed a serum which will coagulate spores of streptothrix. This serum is secured from various mycotic diseases, including blastomycosis, but this, even at its best, can only be used in differentiating mycotic diseases from those of bacterial origin. We tried their methods, but obtained only negative results. We also tried the fixation of the complement according to Wassermann's technique, but the results were not satisfactory. Hence we conclude that agglutination tests and fixation of the complement are of no clinical value in the diagnosis of actinomycosis.

Since practically no work has been done so far on a specific vaccine,[7] we undertook to see what could be done in this line. Our

[6] A Contribution to the Etiology of Actinomycosis, Boston Med. and Surg. Jour., July 21, 1910.

[7] J. H. Wright has told us personally he has tried two cases, Dr. Jensen has used it, and Wynn reported a case successfully treated with a sort of a vaccine.

method was briefly as follows: It is impossible to count the microbes; we took, therefore, three pea-sized bouillon cultures, ground them up in 5 c.c. of normal salt solution and put them in a shaker for twenty-four hours. The mixture was then drawn up into long glass tubes, heated to 80° for three hours, and using this as a stock mixture we made two solutions from it: (*a*) 1 c.c. of the mixture plus 50 c.c. of 0.9 per cent. NaCl plus 2 drops of lysol: (*b*) 4 c.c. of the mixture plus 50 c.c. of 0.9 per cent. NaCl plus 2 drops of lysol. From solution *a*, $\frac{1}{4}$ to 1 c.c. was injected subcutaneously every second and third day, later solution *b* was tried, using 1 c.c. every second day. We never observed any local reaction from these injections. With this vaccine two patients suffering from a severe infection were treated, with the following results.

The first patient was a boy suffering from abdominal actinomycosis and with several large abscesses in the liver. He received five doses of solution *a* at intervals of from two to four days. The injections had apparently no effect, and the case went on to a fatal termination. The second, a man, aged twenty-two years, also suffered from the abdominal type. He had several large abscesses and one had penetrated the bladder. For three months this man received every second day an injection, in the beginning of solution *a* and later of solution *b*. At first he seemed to improve but soon his fever increased, dyspnea appeared and with it cough and pain in the epigastrium. After a few weeks, however, he began to improve and from then on the improvement was steady and marked. To-day he is working and is practically cured, but there yet remains a soft swelling on the left side.

We have then one good result, but of course, no great weight as to the value of the treatment can be placed on it. Further trials with a specific therapy are certainly justifiable.

CONCERNING THE PRESENCE OF THE EMBRYOS OF TRICHINELLA SPIRALIS IN THE BLOOD OF PATIENTS SUFFERING FROM TRICHINIASIS.

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(From the Second Medical Division, Presbyterian Hospital.)

It is now two years since Herrick and Janeway[1] first demonstrated the embryos of Trichinella spiralis in the blood of a patient suffering

[1] Demonstration of the Trichinella Spiralis in the Circulating Blood in Man, Archives of Int. Med., 1909, iii, 203.

from trichiniasis. This most interesting and important finding came as a logical sequence of Staübli's[2] previous experimental work on the mode of dissemination of the embryos in guinea-pigs.

And yet, in spite of the time which has elapsed since this discovery was announced, I have been able to find the reports of but four additional cases.

During the past winter at the Presbyterian Hospital, New York, 4 cases were investigated with special reference to this point. In 2 of these the embryos were found in the blood. In the other 2 several specimens of blood were thoroughly searched, with negative results. Of the negative cases, one was proved to be trichiniasis by the demonstration of the parasites in the muscle, while the diagnosis in the other was never definitely settled.

Trichiniasis is a disease in which the diagnosis may often be made with a fair degree of certainty by the history, physical signs, clinical course, and the eosinophilia, without recourse to the examination of the blood or muscle for parasites. In these well-marked cases there is, perhaps, no great urgency for the use of further means of settling the diagnosis, except in so far as every case is more satisfactory when worked out to the limits of its possibilities.

There are, however, many cases in which the diagnosis is by no means so clear, and in which every means at our disposal must be employed to settle the nature of the disease. Two cases of those reported in this article illustrate this point.

In one, the patient was admitted to the hospital with a diagnosis of typhoid fever. A blood culture being sterile, a Widal negative, and the temperature falling to normal in the course of three days, this diagnosis was abandoned and the case was being considered one of influenza, when an embryo of Trichinella spiralis was recovered from the blood. Subsequent to this the eosinophiles, which had previously not exceeded 5 per cent., rose to 14 per cent.

The other case was even more interesting, although the diagnosis was, unfortunately, never settled definitely. The patient, a woman, was admitted to the hospital with an eighteen-day history of gastro-intestinal symptoms and fever, followed by urticaria and purpura. When admitted, the eruption was marked, but she had no fever. The leukocytes varied between 25,000 and 43,000, and the eosinophiles between 0.3 per cent. and 75 per cent. Her husband was later admitted to the hospital, having been taken ill eighteen days after his wife. A piece of muscle removed from his calf showed many trichinellæ. All possible means of settling the diagnosis in the woman were resorted to. A blood culture was sterile, no ova or parasites were found in the stools, examination of

[2] Klinische u. exper. Untersuchungen über Trichinosis, Verhandl. des Kongress f. klin. Med. Wiesbaden, 1905, p. 351; Beitrag zum Nachweis von Parasiten im Blut, Münch. med. Woch., 1908, lv, 2601; Trichinosis, Wiesbaden, 1909, Verlag von J. F. Bergmann.

the blood for embryos was negative, and a piece of excised muscle showed only "interstitial myositis," similar to that produced by trichinellæ. From the history of the case, the leukocytosis and marked eosinophilia, the muscle findings, and the fact that her husband was suffering from trichiniasis at about the same time, it seems not improbable that the patient was a victim of that disease. The case is interesting from its relation to that little understood group of cases known as "idiopathic purpura." The future examination of the blood for parasites in cases similar to the above may show that in a few the underlying condition is trichiniasis.

Method of Examination. Staübli's[3] original method of diluting the blood with ten volumes of 3 per cent. acetic acid was used, the only modification being that, in several instances, the blood was obtained from the blood cultures taken on the patients. These cultures were the usual routine ones, used in the hospital, 10 c.c. of blood being divided between two Erlenmeyer flasks of meat infusion broth. After the culture had been reported sterile, the clear supernatant broth was decanted and ten volumes of 3 per cent. acetic acid were added to the sediment. The mixture was thoroughly shaken, centrifuged, and the supernatant fluid poured off. If the resulting sediment was too thick, the laking with the acid was continued until a sediment was obtained in which the search was unhampered by the presence of countless numbers of blood cells. A drop of the sediment was then poured on a large slide, covered with a good-sized cover slip, and systematically searched with a low-power lens.

The embryos appear as a distinct, cylindrical, generally slightly curved little worms, with a refractile outline and a characteristic granular internal structure. Both ends are somewhat rounded. The anterior end is a little narrower than the rest of the body, and ends in a little, clear, homogeneous cap. The obliquely placed clear band, mentioned by Staübli,[4] as forming a line of demarcation between the anterior quarter and posterior three-quarters of the body, was not observed in the embryos studied. According to him, this band is especially well seen in the stained preparations (see illustration). Foreign substances in the sediment, such as cotton fibers, thin plugs of red cells, and fungus growths, may at first cause some confusion, but when once seen, the embryos are quite characteristic.

The embryos found in the present cases measured from 0.005 to 0.007 mm. in breadth and from 0.1225 to 0.1295 mm. in length.

By rimming the cover slip with vaseline or cement, the preparation may be preserved for several weeks.

[3] Verhandl. des Kongress f. klin. Med. Wiesbaden. 1905, p. 354; Münch. med. Woch., 1908, lv, 2601.

[4] Trichinosis, Wiesbaden, 1909, Verlag von J. F. Bergmann.

Numerous smears of the sediment were stained by various methods, but none of the parasites could be found. Herrick and Janeway had a similar experience. Staübli, however, had no difficulty in obtaining stained specimens which show the clear band at the anterior part of the parasite very distinctly.

None of the parasites was found in the stools.

The following is a brief review of the cases examined. They were all admitted to the Second Medical Division, and I am indebted to Drs. James Kinnicutt and Bovaird for permission to use the clinical facts here given.

Fig. 1.—Embryo of trichinella spiralis in blood sediment from Case II. The microphotograph was taken by Dr. Hugh Auchincloss, New York.

Case I.—A woman, aged twenty-nine years, was admitted to the hospital on December 21, 1910. Eighteen days before admission, while working in the house, she was taken suddenly ill with pain in the upper part of her abdomen. This pain was severe, gnawing, continuous, and without radiation. At times her whole abdomen was tender. She had severe diarrhea, ten to twelve movements a day, the stools being foul and watery, but containing no blood. With the onset of pain, she complained of headache. She suffered from these symptoms much of the time for nine days, when she entered the Norwegian Hospital, where it was at first thought that she was suffering from typhoid fever. During the week that she remained there she suffered from soreness and stiffness of the left side of her

neck. There were two epistaxes. All of her symptoms cleared up and she left the hospital feeling well. Three days before admission to the Presbyterian Hospital, after drinking a glass of wine, the pain in her abdomen returned. It was relieved by vomiting and did not again appear. Two mornings before admission she noticed itching of her legs, and found them covered with large, raised, white blotches. The next day the eruption appeared about her waist, and on the morning of admission on her arms.

Physical Examination. Old herpes on lip. No puffiness of the face. Spleen not palpable. There is a remarkable purpuric, and in places ecchymotic, rash covering a large part of her body. The face, thorax, and upper part of the abdomen are not involved.

There was at no time any muscular tenderness. She had no fever. The rash gradually faded in the course of a week, but not without the appearance of fresh spots. She left the hospital on January 17, in good condition.

Seven blood counts showed a leukocytosis varying between 25,000 and 43,000, and an eosinophilia between 0.3 per cent. and 75 per cent. On several examinations no ova or parasites were found in the stools. A blood culture taken on admission was sterile and no parasites were found in the blood sediment from this culture.

Three days after admission 10 c.c. of blood were drawn from an arm vein and examined for parasites, but with negative results.

Three weeks after admission a piece of muscle was excised and examined. The pathologist returned the following report: "Between the muscle bundles is a slight increase in the fibrous tissue in spots and deposits of small numbers of lymphoid cells. The changes are similar to those produced by trichinæ. No trichinæ found. Diagnosis, interstitial myositis, probably due to trichinæ."

Case II.—A man, aged twenty-nine years, was admitted to the hospital December 29, 1910, with a history of malaise and chilliness for nine days. Four days before admission he went to bed with these symptoms, plus general muscle pains and swelling of the face and hands. He had no gastro-intestinal symptoms at any time. His brother was taken ill at the same time, and it was found that they had both eaten pork of their own cooking shortly before the onset of their illness. The brother entered a hospital in Pennsylvania, and it was impossible to obtain a specimen of blood for examination.

Physical examination showed nothing abnormal except a fine, punctate rash over the abdomen, thorax, and arms.

For three days he had a temperature in the neighborhood of 103°, gradually falling to normal.

The blood count showed 10,000 leukocytes and 11.5 per cent. of eosinophiles. A blood culture taken on admission was sterile. From this culture four embryos were found.

The patient refused permission to excise a piece of muscle.

CASE III.—A man, aged thirty-four years, the husband of Case I, was admitted to the hospital on December 31, 1910, with a ten days' history of malaise, chilliness, and indefinite pains in the back of his neck and in his limbs. At times he noticed puffiness of his eyes. He had eaten pork three weeks before admission.

Physical Examination.—There is no puffiness of the face. He holds his head well turned to the right. Rotation causes pain in the posterior neck muscles, which are, however, not tender to pressure.

He had a temperature of 104°, gradually falling to normal in the course of three days.

His leukocytes varied from 15,000 to 23,000, and his eosinophiles from 2 per cent. to 41.3 per cent. The blood culture taken on admission was sterile. An examination of all the sediment from this culture was fruitless.

On January 5 a piece of muscle was removed from the calf. It was found to contain many embryos.

Following this finding another search of the blood was made on January 9. Ten c.c. of blood were drawn from an arm vein directly into 3 per cent. acetic acid. No embryos were found in the sediment.

CASE IV.—An Italian, aged twenty years, was admitted to the hospital on January 5, 1911, complaining of backache and general malaise for five days and indefinite pains in the bones, joints, and back for three days. At times he had rather mild colicky pains in his abdomen. Had some fever.

Physical examination showed slight puffiness of the eyelids and cheeks, a coated tongue, palpable spleen, and a few fine, reddish, punctate spots over the abdomen and chest. There was no muscular tenderness.

His temperature on admission was 104.4°, gradually falling to normal in the course of a few days.

Three blood counts were taken, as follows: January 5, leukocytes, 12,000; eosinophiles, 3 per cent. January 7, leukocytes, 12,400; eosinophiles, 5 per cent. January 12, leukocytes, 15,600; eosinophiles, 14 per cent.

A blood culture taken on admission was sterile. From this one embryo was recovered:

The patient would not consent to the removal of a piece of muscle.

There follows a list of the cases so far reported, together with those of the present series:

1. Herrick and Janeway.[5] April, 1909. They investigated 8 cases in one family. In 4 the blood was examined, but in 1 only were the embryos found. In that case they were found on two different occasions, on the tenth and twelfth days after the onset.

[5] Loc cit.

2. Packard.[6] April, 1910. The embryos were found in the blood twenty-two days after the onset. They were recovered from the muscle "a few days" later.

3. Barach and Mercur.[7] May, 1910. The parasites were found in the blood fourteen days after admission. The time of onset was not given. Sixteen days after the parasites had been found in the blood they were recovered from the muscle.

4. Cross.[8] September, 1910. Three embryos found on the eighth day after the onset. In this case only 1 c.c. of blood was taken. It was drawn from the lobe of the ear. Cross suggests that "it may be easier to obtain the parasites from the mixed arterial and venous blood than in the blood which has traversed the capillaries and is taken from the vein."

The patient would not consent to the removal of a piece of muscle.

Cases of the Present Series. 1. No embryos found on the nineteenth and twenty-second days after the onset. Six weeks after the onset a piece of muscle showed only "interstitial myositis."

2. Embryos found on the ninth day after onset. Muscle not examined.

3. Search for embryos negative on the thirteenth and nineteenth days after onset. Found in the muscle fifteen days after onset.

4. Embryos found on the sixth day after onset. Muscle not examined.

From the above it will be seen that the earliest time at which the embryos were found was on the sixth day after onset, and the latest twenty-two days after the beginning of the disease. In these cases the time of onset has been taken as the only available fixed date. It has many disadvantages over Staübli's method of reckoning from the time of eating the trichinellous meat. But he was dealing with animals where the date could be easily ascertained, whereas with human beings it is very difficult to find out at what time they have eaten infected material. Indeed, it is often impossible to obtain a history of having eaten such material at all.

Staübli,[9] from his experiments with guinea-pigs, concludes that the birth of the embryos begins, at the earliest, six or seven days after infection, and that the maximum migration in the blood lies between the eighth and twenty-fifth days after eating the infected meat. He was unable to find embryos in the heart blood of guinea-pigs later than the twenty-seventh day after infection.

The variation in the incubation period of the disease is so great that it is impossible to accurately correlate the figures given above

[6] Trichinella Spiralis in Human Blood, Jour. Amer. Med. Assoc., 1910, ii, 54, p. 1297.

[7] A case of Trichinosis with Recovery of Parasite from the Blood and Muscle, Archives of Int. Med., 1910, v, 530.

[8] A Case of Trichinosis; Trichinella Found in Blood Taken from an Ordinary Ear Puncture Archives of Int. Med , 1910, vi, 301.

[9] Trichinosis, Wiesbaden, 1909, Verlag von J. F. Bergmann.

with those of Staübli. However, in general, it may be said that the time of maximum migration agrees fairly well in the two sets of cases.

Braun[10] is authority for the statement that the adult parasites continue to live and give off embryos for from five to seven weeks. This would certainly indicate that it may be possible to find the embryos in the blood at a later date than those given above.

There seems to be an impression that it is useless to search for the parasites in the blood after they have been found in the muscle. While no cases have been cited to prove the contrary, Packard found them in the blood only "a few days" before their recovery from the muscle. The first embryos reach the muscle on about the ninth or tenth day after infection, leaving a period of from two to three weeks when there is still a fair chance of recovering them from the blood.

Conclusions. 1. In the examination of the blood sediment for the embryos of Trichinella spiralis we have a valuable means of diagnosis in cases suggesting trichiniasis.

2. From the meagre number of cases so far reported, it would appear that the method had not been used as frequently as its value would merit. It must be remembered, however, that even under favorable conditions, this method is not infrequently unsuccessful.

3. The technique of the examination is very simple. While the search for the embryos is tedious, it is scarcely more so than the examination of the blood for the plasmodium of malaria.

4. The earliest time at which the embryos may be found in the blood is on the sixth or seventh day after infection. The latest date is not so accurately fixed. While the parasites have not been found later than the twenty-seventh day after infection in guinea-pigs, or later than the twenty-second day after the onset of symptoms in man, there is some ground for the belief that they may occasionally be recovered in the fifth or possibly the sixth week after infection.

5. This method is of greatest value in those cases where the diagnosis is doubtful and especially where the patient refuses permission to excise a piece of muscle or where the muscle findings are negative.

[10] Die Tierischen Parasiten des Menschen, Wurzburg, Verlag von A. Stuber, 1908.

BACTERIN TREATMENT OF SEPTIC RHINITIS OF SCARLET FEVER, WITH REPORT OF ONE HUNDRED CASES.[1]

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Since the exact cause of scarlet fever is unknown, the problem of infection and the illness of the "return case" is very perplexing. Until comparatively recent times the desquamated epithelium was regarded as the chief infectious agent. Gradually the infectious character of discharges from the upper air passages and especially the nose is being recognized. However, until the exact contagium is discovered to explain some of the paradoxes of infection in scarlet fever, the question of infection will always be in doubt. While many of those having considerable experience with the hospital management of scarlet fever may be dubious of the infectiousness of the epithelium of late desquamation, everyone recognizes the danger lurking in discharges from the upper air passages.

In this connection, the report on "return cases "of the Metropolitan Asylums Board[2] of London is of much interest. This report shows that, of 1361 patients discharged from the hospital with some evidence of desquamation, only 94 cases, or 14.5 per cent., were associated with the illness of "return cases," and in the majority of these "infecting cases" another morbid condition co-existed which was sufficient in most instances to account for the illness of the "return case." For instance, in 60 cases a morbid condition of the nose or postnasal region existed. In only 24 cases was desquamation alone present. On the other hand, there were 125 "infecting cases," equivalent to 19.2 per cent., in which apparently no morbid condition, as desquamation or nasal discharges, was present. So that, whatever may be said of the early desquamation, the evidence adduced would seem to show that the late desquamation is not infectious. The same report shows that in 52 per cent. of cases a morbid condition of the nose was the lesion associated with the illness of a "return case." This percentage agrees closely with the records of the Philadelphia Hospital for Contagious Diseases, and emphasizes the important relation between the nasal discharges of convalescents and the spread of scarlet fever.

[1] Read by invitation before the Philadelphia County Medical Society, April 12, 1911.

[2] Metropolitan Asylums Board. A Report of Return Cases of Scarlet Fever and Diphtheria, Henry Kemmshead, London, 1902, p. 19.

Nasal discharge in scarlet fever patients are usually very persistent and refractory to treatment. While bacterin therapy has been used with success in both acute and chronic rhinitis of non-scarlatinal origin we have not been able to find any reference to its use in the treatment of the rhinitis of scarlet fever. This report is based upon the bacterin treatment of one hundred such cases of septic rhinitis, treated in the scarlet fever wards of the Philadelphia Hospital for Contagious Diseases.

Many patients have discharging noses early in the disease when admitted to the hospital, others develop the condition shortly after admission, but in the large majority of cases this purulent or non-purulent rhinitis develops during convalescence, frequently just preceding dismissal from the hospital. The nose is always most carefully examined by Dr. Woody, chief resident physician, three different times before the patient is permitted to go home, and if only suspicious of discharge the patient is detained in the hospital. In this way the period of residence in the hospital is frequently much prolonged.

It is a difficult matter to adopt a good working classification of these nasal conditions. We have divided them for convenience into purulent and non-purulent rhinitis. The former is characterized by a profuse mucopurulent discharge which produces considerable excoriation about the nostrils and upper lip. The lower turbinates are congested and edematous and covered with this glairy purulent material. Crusts form about the nostrils, and the child invariably picks at these, soon producing a swollen, bleeding, crusty, painful condition. Children under four years of age cannot cleanse their noses by blowing, and irrigation is dangerous and often impossible. Splinting the elbows or tying the hands in mittens to prevent picking, with simple cleansing and the application of protective and soothing ointments, is about all one may do. The course of the disease in the majority of these cases is frequently prolonged and most tedious. Less severe cases show swelling of the turbinates with a small fissure at the mucocutaneous junction, with a thin, watery, scalding discharge.

In the non-purulent cases the turbinates are enlarged and the discharge is profuse, thin, and watery, or mucoid, and irritates the nostrils and upper lip. In the mildest cases there is present a moisture about the anterior nares, with redness and tenderness of the nose. We endeavored to separate ordinary acute colds, in which the discharge is purely mucous, from the rhinitis under discussion, in which the discharge is more apt to be serous or seropurulent, septic, and very irritating in character.

We believe that this rhinitis is, in itself, specifically infectious. Kerr[3] states that "it is undoubtedly infectious from patient to

[3]Text-book of Infectious Diseases, Oxford Med. Press, first edition, 1909.

patient and plays a prominent part in the production of the return case." We have noted, on two different occasions, an outbreak of this rhinitis in a convalescent ward of patients with healthy noses, to follow in from two to four days the introduction of a rhinitis case from another ward. Adenoids especially predispose, and these complicated cases resist all treatment. The younger and weaker patients are quite prone to suffer with this septic rhinitis. The warm bath preceding dismissal from the hospital has been a fruitful source by lowering both general and local resistance. Since this has been eliminated by giving the disinfecting bath on the day previous to discharge, fewer cases develop rhinitis prior to discharge or upon reaching their homes.

What part does nasal discharge play in the etiology of "return cases" of scarlet fever? Some persons believe that these discharges are not infectious *per se*, but rather that the scarlet fever infection is derived from acute cases and engrafted on the patient. Simpson[4] points out "that the infection, the causal microörganisms, appears to acquire activity particularly in the mucous discharges, whether acute or chronic, but further than acting as suitable media for their growth and carriers of any possible infection that may come in contact with them the discharges do not appear to possess infectious properties of themselves."

If the secretion dries up, there is no longer the medium on which the microörganisms can engraft themselves, so that the patient becomes non-infectious.

Others believe that the "infecting case" at the time of dismissal has not entirely eliminated the infection derived from the original attack, and as a consequence the discharges remain infectious. This view is hardly tenable. We are led to agree with the views of Cameron,[5] who believes that the causal microörganisms of scarlet fever lead a saphrophytic existence in the mucous membranes, and when conditions are favorable retain their vitality for a considerable period of time. In most cases the conditions are unfavorable and the infection dies out, but in other cases it may live and retain its vitality, especially upon a mucous membrane impaired either by a general lack of vigor or by a superadded local, septic infection. For this reason an "infecting case" may be one of poor vitality without a local lesion in the nose, and this agrees with the clinical observation that a discharge is not necessary to the patient's infectiousness. This superadded septic infection may be acquired either before or after admission to the hospital by extension of infection from the throat, inhalation of dust, etc. A warm bath followed by chilling of the body may so lower vital resistance as to favor activity of septic organisms in the mucous membranes.

We began the bacterin treatment of these cases with the hope of

[4] Metropolitan Asylums Board Report, p. 52.

[5] Ibid, p. 54

overcoming this septic infection, and not with the idea of combating the causal agent of scarlet fever itself. We believe that this scarlet fever agent, whatever it may be, will die if the superadded septic infection is removed.

Excellent work has been done on the bacteriology of the normal nose and also of its inflammatory diseases. Our work is confined entirely to these cases of septic rhinitis complicating scarlet fever. We were surprised at first with the great regularity in which staphylococci were found, usually aureus, and practically in pure culture. We felt that possibly our technique was faulty and that some of the organisms might have escaped detection Accordingly the various methods and media which have been advised from time to time for isolation of streptococci, pneumococci, and the influenza and diphtheroid group of bacilli were employed. But, as will be seen, our findings include but four organisms: Staphylococcus aureus occurred alone in 89 cases; Staphylococcus albus in 3 cases; a diphtheria-like bacillus in 6 cases; Staphylococcus aureus and a diphtheria-like bacillus occurred together in 1 case; and Staphylococcus aureus and Streptococcus pyogenes were found associated in 1 case.

The staphylococci and Streptococcus pyogenes were isolated and classified according to cultural and biological characteristics. Special attention was given the diphtheria-like organisms because of their relation to the Klebs-Loeffler and Hofmann's bacillus. As will be noted in the tables, they were found in 7 per cent. of the cases. In every instance the organism was of medium length, solid, with rounded or slightly pointed ends, evenly and darkly staining, Gram positive, and in four instances showing a faint median band. Unfiltered bouillon cultures and filtered toxins grown for forty-eight hours were made and injected subcutaneously into guinea-pigs in doses corresponding to 0.5 per cent. of the body weight of the animal expressed in cubic centimeters. All gave negative results. Three cultures were inoculated into tubes containing Hiss serum water media containing 1 per cent. of dextrin, maltose, mannite, lactose, and saccharose respectively. In one case acid was produced in dextrin and maltose, indicating the true diphtheria bacillus, the other two yielded negative results, indicating Hofmann's bacillus.

The following table gives the duration of the septic rhinitis prior to culturing and the first dose of bacterin:

	Cases.
Two to four days	48
Four to seven days	19
Seven to twelve days	16
Twelve to twenty days	6
More than twenty days	11

Cases of nasal discharge were reported to us on the second or third day of discharge. The case was then examined and the ques-

tion of the advisability of bacterin treatment considered. A culture was then made, and in a large number of cases a dose of stock polyvalent Staphylococcus aureus vaccine was administered at once. In many cases this was the only dose required, but all cases were cultured in order to detect the presence of some organism other than the Staphylococcus aureus. If two organisms were found they were isolated and a separate bacterin of each prepared. The aggregate dose of the two bacterins equalled the usual dose of one. The size of a dose depended upon the general condition of the patient; the younger and weaker receiving correspondingly smaller doses. The initial dose varied from 50,000,000 to 100,000,000 of staphylococci and 50,000,000 to 80,000,000 of the diphtheria-like organism. Succeeding doses were given every five to eight days, depending upon the clinical aspect of the patient. Injections were given in the loose areolar tissue of the back by means of an all-glass sterilized syringe. All other treatment was stopped except cleanliness of the parts and application of soothing ointments. Other infections, toxemia with fever, nephritis, and low vitality were considered contraindications. The following table gives the number of doses administered, with the results obtained:

Doses.	Cases.	Cured.	Improved.	Not improved.	Other infections.
1	43	39	1	2	1
2	29	23	3	1	2
3	12	9	1	2	
4	6	3	1	2	
5	6	2	2	2	
6	3	1	..	2	
7	1	..	..	1	

The temperature reaction following the injection was moderate, reaching 100° to 102° F., and falling to normal in twenty-four to thirty-six hours. We never had an abscess. There is usually a slight local redness and tenderness and general malaise following the injection. In the majority of cases the discharge begins to lessen after twenty-four hours. The congestion of the turbinates was relieved quite promptly, and in two to four days bad cases were well. If no improvement followed three doses, another culture was made and a bacterin prepared. Examination was also made for the presence of adenoids. If these were present, bacterin treatment was stopped, as treatment in such cases has proved to be valueless. In the first few cases of adenoids, extensive treatment was persisted in, but to no avail. All cases were retained in the hospital from four to ten days after the rhinitis had cleared up.

It is a difficult matter to draw an impartial conclusion concerning the value of bacterin treatment in these cases of septic rhinitis. In individual cases the results were most striking, when we naturally expected a prolonged course would follow under ordinary treatment. This rhinitis occurs in from 10 to 20 per cent. of cases and is usually persistent. Many cases heal promptly with usual

treatment, but the time required for such a result is very much decreased with bacterin treatment. We have not been able to trace one "return case" which can be attributed directly or remotely to one of the cases that received bacterin treatment.

Examination of the last table shows a cure in 77 per cent. of cases; 8 per cent. were improved, 12 per cent. not improved, and 3 per cent. contracted other infections, and the treatment was stopped. The 8 cases showing improvement had a very slight discharge when dismissed; 9 of the cases not improved had adenoids, and 3 were of poor vitality; 1 patient developed pertussis, 1 Vincent's angina, and 1 acute scarlatinal nephritis. All cases not cured were held at least four weeks over the usual period of residence in the hospital.

For the sake of comparing the efficacy of stock and autogenous bacterins, about an equal number of cases were treated with each. The stock bacterin was made from twelve different cultures of Staphylococcus aureus. All bacterins of the diphtheria-like bacillus and the Streptococcus pyogenes were autogenous.

Cases treated with	Cured.	Improved.	Not improved.	Other infections.
Autogenous bacterins, 52 . .	35	6	10	1
Stock bacterins, 48 . . .	43	2	1	2

All the adenoid cases were treated with autogenous bacterins, which accounts for the apparently better results with the stock bacterins. The results were about equal.

Conclusions. 1. That nasal discharges are of primary importance in the etiology of the "return case" of scarlet fever.

2. That the true rhinitis of scarlet fever is septic in character, distinctly infectious in itself, and probably harbors the contagium of scarlet fever.

3. That bacterin treatment of cases of septic rhinitis is more satisfactory than the usual treatment. It shortens materially the time required for cure and decidedly aids in decreasing the number of "return cases."

CHRONIC PNEUMONIA (INCLUDING A DISCUSSION OF TWO CASES OF SYPHILIS OF THE LUNG).

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Among the numerous indurative processes in the lung, chronic (unresolved, organizing, or indurative) pneumonia is specially interesting from the high frequency of complications, and especially on account of the irregularity of its clincial symptoms and the

uncertainty of its diagnosis and prognosis. Owing to this uncertainty, the diagnosis is, it might be said, as a rule, mistaken, and it also perhaps accounts for the rather incomplete clinical data relating to this disease.

Of a series of 159 cases of pneumonia which came to autopsy in the Russell Sage Institute, New York (95 lobar and 65 bronchial), 10 (6 males and 4 females) illustrated examples of this organizing type. In 9 of these, whole lobes or at least large areas of the lung were affected, and in only 1 was the process more patchy in character and more definitely bronchopneumonic in distribution.

These 10 cases represent examples of pneumonia where the usual process of resolution has failed and organization of the inflammatory exudate in the air alveoli of the lung by fibrous tissue has resulted.

Such conditions of non-resolution and fibrous organization of acute pneumonic processes have been recognized as a clinical and pathological entity for some considerable time, particularly by German writers; yet in English literature it has occupied only a relatively slight interest, either as regards its clinical importance or its pathological distinctive features. Laennec[1] in 1819 was perhaps the first to observe this type of disease. He considered that the lung presented in these cases a greater hardness, was more regular, and a more gray-violet, livid red color than in simple hepatization. Andral in 1837 described somewhat similar appearances, and Stokes in 1838 noted definitely a case of pneumonia as having become chronic after one month's duration of the acute condition. Lebert[2] in 1857 spoke of a "transformation fibreuse" of the pneumonic exudate, and Rokitansky in 1861 advocated the possibility of a simple hepatization becoming hardened into an "indurierte Hepatisation" and also of "neugebildeten Bindegewebes-elementen welche den Elementen des Eiters und den aus den Eiter und Epithelial-zellen hervorgegangen Fettkörnchenzellen bei der Hepatisation oder eitrigen Infiltration beigemischt sind." In the text-books of Birch-Hirschfeld (1877), Jurgensen (1878), and Niemeyer-Seitz (1879) the possibility of a sequence of an "interstielle Pneumonie" after the acute croupous form is admitted. Virchow demonstrated the process of induration to be a vascularization and organization of the exudate, and applied the term "carnification" to the result ("Die Form der Induration welche die Alveolen ausfüllt, als Carnification").[3] Corrigan described "cirrhosis pulmonum" as a special disease, *sui generis*, analogous to liver cirrhosis, and Clark[4] came to a similar conclusion, noting also that "all cases of fibroid phthisis were not due to tubercle." Rindfleisch, Amburger,[5] and Hanau[6] were of the same opinion, as also was Balzer,[7] who described this special process as a "pneumonie chronique recurrente." Heitler[8] agreed that this chronic pneumonia was a distinct entity, and was developed from a "paren-

chymatous pneumonie." Buhl also strenuously denied any relationship to any acute condition, and he believed it commenced as a "desquamative pneumonia," and that, as regards croupous pneumonia, only capsulation or cicatrization around abscesses or gangrene was possible. Wagner[9] was not so definite, as he admitted the connection between acute and chronic pneumonia, but was not sure of any relationship between acute croupous pneumonia and the chronic indurated condition. Borrmann[10] also considered it risky to think of every case as arising as a special process and not as a sequence of acute pneumonia. Heschl,[11] Woronochin, Ackerman,[12] Eppinger,[13] and the majority of more recent authors, Leyden,[14] Lindemann,[15] Kidd,[16] v. Kahlden,[17] Aldinger,[18] etc., have followed Marchand[19] in his views that these cases of organizing pneumonia are sequels of an acute pneumonic process, and an event which may follow the acute croupous form ("das eine nachfolgende frische, croupöse Pneumonia, denselben Ausgang in Induration nimmt").

A variety of explanations have been advanced as to why this organization and not the usual process of resolution should occur in some pneumonia cases. Heschl has observed this transformation particularly in wasted individuals; Cornil and Ranvier and Marchiafava[20] found this type especially in very old, feeble subjects. Hart,[21] however, found well-marked organizing processes following bronchopneumonia associated with measles, and Ziegler described a similar event. Marchand considered it more frequent in alcoholics and Josephson[22] in alcoholic, defectively nourished subjects. Amburger advocated syphilis as the essential factor. Ziegler[23] considered the probability of recurring exudates eventually requiring organization for their removal, and Jurgenson that preëxisting congestion was of etiological moment. Eppinger and Cohn,[24] and to some extent Marchand, thought that pleural adhesions limiting the respiratory movements of the lungs and causing congestion were essential. According to von Kahlden,[25] obstruction of the bronchial tubes and resulting retention of unexpectorated exudate was important. Köster[26] showed the etiological importance of the lymph channels being clear if resolution is to take place successfully, and v. Kahlden has applied this to emphysema, where the walls of the air spaces are thin and their vascular and lymphatic channels naturally defective for absorption and resolution.

In a review of the 10 cases on which the present communication is based, it was seen that in 2 the pneumonic process was situated in the upper lobe of the right lung, one in the upper and middle lobes of the right lung, 1 in irregular patches throughout the right lung, in the middle lobe of the right lung, with extension into the adjacent upper and lower lobes, 1 in the lower lobe of the right lung, and 4 in the lower lobe of the left lung. These locations then do not conform to the common statement that apical pneumonias are specially subject to delayed resolution. With two exceptions all

the cases occurred between the ages of sixty and ninety-two years. In this connection, however, it has also to be noted that in the remaining 149 cases of pneumonia a similar proportion also occurred within about the same age limits.

The question of emaciation was also apparently of indifferent importance, as 4 of the cases were comparatively well nourished.

Likewise alcoholism, and certainly syphilis or tuberculosis, did not play an essential part, as in only 3 of the 10 cases was there any history of syphilis, and in 2 small healed foci of tubercles were found in the apices of the lungs.

Emphysema was considerably more important, yet the lungs in 7 at least of the 9 cases were only moderately emphysematous, and on microscopic examination the alveolar walls did not seem to be especially atrophied.

Nephritis and general arteriosclerosis were also in no degree constant, nor was there any special chronic cardiac condition or marked general venous stasis.

Eppinger and Cohn's ideas of the essential feature of pleural adhesion and thickening also could not be sustained, as in most of the cases there was no such fixation of the lung.

Occasionally some of the smaller bronchi were obstructed, but the process was coincident with the alveolar organization, and certainly did not necessarily precede it, as several authors have advocated.

One factor, however, as will be seen from the following synopses, was uniform in all the cases, that being their extreme debility, either from some preceding or coexisting disease.

Case I.—An extremely emaciated man, aged sixty-eight years, who had entered the hospital in a state of extreme debility, and died shortly afterward. He had been confined to bed for about a month previously, but nothing further could be ascertained. The autopsy showed an organizing pneumonia of the lower lobe of the right lung, with also, as in all the other following cases an overlying subacute pleurisy.

Case II.—A somewhat emaciated man, aged seventy-five years, who had suffered from dyspepsia due to carcinoma of the pylorus for seven months. At no time did he ever have any symptoms which might have been related to pneumonia. The temperature remained normal until the last four days of life, when it rose to 100°, and remained about this level. During the whole fourteen days in hospital there was dulness noted corresponding to the lower lobe of the left lung, and over this area faint bronchial breathing without any accompanying rales was heard. At autopsy the lower lobe of the left lung was consolidated and fleshy in consistence from organizing pneumonia.

Case III.—A fairly well nourished man, aged sixty-five years, who entered hospital extremely debilitated, in the convalescent

state of facial erysipelas, which had started three weeks previously. Beyond this no definite history relating to pneumonia could be determined. On first examination his leukocytes numbered 16,500 per c.mm., and there was definite dulness and bronchial breathing over the middle lobe of the right lung. He lived twelve days after his admission to hospital, the temperature, at first 102.6°, continued to swing irregularly, with a maximum of 103°, and toward the end, as evidences of empyema developed, an incision was made just anterior to the right nipple, and a loculated pneumococcal empyema over the outer part of the middle lobe of the right lung was drained. At autopsy there was a small gangrenous patch in the middle lobe, which communciated with the empyema cavity. The rest of the middle lobe was in a condition of organizing pneumonia, as was also the lower part of the adjacent upper lobe.

Case IV.—A fairly well nourished man, aged sixty-three years, who presented an alcoholic history, and for the last thirteen years had occasional attacks of cardiac insufficiency and anasarca from chronic nephritis. Forty-two days before the date of his death, after two days' exposure in an alcoholic condition, he experienced sudden chills and pain in the left side of the chest. On his entrance to hospital ten days after the onset of these symptoms there was definite bronchial breathing, some fine crepitations, and fine friction rales over the lower lobe of the left lung. The leukocytes numbered 22,000 per c.mm. (82 per cent. polymorphs). Ten days later a pericardial friction rub became evident, and the heart's action assumed a gallop rhythm. The leukocytes at this time numbered 8000 per c.mm. The temperature had a daily range of between 102.5° and 99° as an average during the whole thirty-two days in hospital; the pulse averaged 100, and respirations 28 throughout. At autopsy there was an organizing pneumonia of the lower lobe of the left lung. The left pleural cavity contained a small amount of turbid fluid, from which pneumococci were isolated. The right pleural cavity also contained a small amount of clear fluid. There was also a fibrinous pericarditis, the pericardium containing a small amount of turbid fluid, in which pneumococci could be demonstrated, and the surface of the heart was entirely covered by a shaggy fibrinous exudate.

Case V.—A somewhat emaciated man, aged thirty-two years. When twenty years of age he had a chancre, but no secondary eruption. Seven years later he developed a gradually advancing hemiplegia, which was complete in three months. On admission to hospital he presented a complete right spastic paralysis, and his heart was markedly enlarged from aortic incompetence. During the six weeks he was in hospital the temperature remained normal, pulse averaging 80, and respirations 22. He did not complain of any symptoms referable to the respiratory system except some occasional fits of coughing. Twenty-one days before death, however,

a fine friction rub became evident over the upper part of the right interscapular region, and on deep respiration there was some catching pain over the upper part of the right side of the chest. No sputum was expectorated. Over the upper lobe of the right lung dulness and high-pitched bronchovesicular breath sounds developed. Two days before death he suddenly developed typical signs of meningitis. Coincidentally, the temperature, previously normal, rose to 105.5°, and the leukocytes rose to 32,000 (58 per cent. polymorphs) from a previous maximum of 14.500 per c.mm. Toward the end the hemoglobin had fallen to 58 per cent., and the red blood corpuscles to 3,597,000 per c.mm. At the autopsy the upper lobe of the right lung, with the exception of the extreme apex, was carnified from chronic pneumonia. The brain and spinal cord showed a marked purulent pneumococcal meningitis, the pus being chiefly aggregated over the vertex of the cerebrum. There was also an old atrophy of the left Rolandic area of the brain, due to old thrombosis, and the aortic valves of the heart were incompetent from chronic endocarditis.

Case VI.—A well-nourished woman, aged ninety-two years, whose only obtainable history was that she had been hemiplegic for some years, and had been latterally for some months confined to bed. Clinically the presence of fluid in the right pleural cavity was suspected, but the temperature, pulse, and respiration, although not fully recorded, were not abnormal until the last two days of life, when the temperature rose slightly. At autposy about 15 ounces of a thin fluid, from which a pneumococcus and staphylococcus albus were isolated, was found in the right pleura. There was an organizing pneumonia of the lower lobe of the right lung, and the organization in this case was comparatively advanced and fibrous. The pericardium contained a small amount of slightly turbid fluid, and there were patches of recent fibrinous deposit on the surface of the heart, particularly near the base. (As no organisms could be discovered in the pericardial exudate, it was difficult to establish the absolute relationship of the process). The kidneys (left, 150 grams; right, 115 grams) showed some arteriosclerotic atrophy, and there was an old thrombosis of the left middle cerebral artery, with atrophy of the convolutions of the Rolandic area and under surface of the temporosphenoidal lobe on the left side. In this case the duration of the pneumonic process was not determined, but evidently from the advanced state of the organization it must have existed for some considerable time.

Case VII.—A poorly nourished woman, aged sixty years, who had entered hospital complaining of cough and breathlessness, which had followed a severe cold contracted three weeks previously. During these three weeks she had been under the influence of alcohol almost continuously. Two days before admission

to hospital she suddenly became very feverish, and her breathlessness much more marked. When first examined in hospital there was an indefinite dulness, with harsh vesicular breath sounds and prolonged expiration, accompanied by numerous moist crepitations over the lower part of the left side of the chest. Over the upper lobe of the right lung there was definite dulness and fairly loud bronchial breathing. There was a soft systolic mitral murmur transmitted out into the axilla. The leukocytes numbered 24,000 per c.mm. (85 per cent. polymorphs), and the temperature was 102°, pulse 100, and respirations 34. The sputum was yellow, tenacious, and contained numerous pneumococci. The temperature gradually rose to 104° on the fifth day and came down by lysis to 100° on the eighth day. It varied between 100.5° and 99° for the next six days, when it again rose to 101.5° (sixteenth day), returning to 99° the next evening. At this period the leukocytes numbered 32,000 (83 per cent. polymorphs). The temperature continued varying between 99.6° and 98.2° until the twenty-first day, and since then until the twenty-eighth day, when death occurred suddenly, the temperature remained within normal limits. During the whole time in hospital the respirations averaged 26 or 48 per minute, and were not particularly labored. At autospy it was found that the lower lobe of the left lung was edematous, congested, and bound down by numerous stringy adhesions. The lower two-thirds of the upper lobe of the right lung showed an organizing pneumonia, and over its surface was a subacute pneumococcal pleurisy. The pneumonic area was fleshly in consistence, dark brownish red in color, and included numerous grayish streaks and spots. The pericardial sac was separated from the heart by a thick layer of creamy pus, in which numerous pneumococci were demonstrated.

Case VIII.—An emaciated male, aged seventy years, who had come to hospital for a severe ulcerative stomatitis. He was not specially alcoholic, and he denied any previous illnesses. At this time his lungs were reported as generally emphysematous. Two months later he developed double otitis media, for which a radical mastoid operation was performed on the right side. The temperature, which had developed with the onset of the middle ear disease, continued irregularly, varying between 100° and 102° for ten days after the operation. Six weeks later (four days before death) the temperature again became irregular, reaching up to 102°, but falling the next day to 97°, and remaining until the end at about 99°. At no time was the pulse or respiration rate apparently altered from normal, and he presented no symptoms relating to his respiratory system. The diagnosis of pneumonia was not made, and he died in extreme asthenia, having emaciated very markedly in the last month.

At autopsy both middle ears and mastoids were filled with a large amount of greenish-yellow pus, containing staphylococci and

streptococci, and from the right mastoid a sinus communicated externally. There were numerous encapsulated trichinæ in the chest and abdominal muscles. No fluid was contained in either pleura. The lower lobe of the left lung was fleshly in appearance, from organizing pneumonia, and over its surface was a thin patchy layer of subacute pleurisy. Throughout the pneumonic area in this lung were numerous miliary abscesses.

Case IX.—An emaciated man, aged sixty-eight years, who had an alcoholic history, and who had entered hospital complaining of dizziness, cough, and defective vision. Two days later the temperature slowly rose to 101°, and next day reached 104.4°. At this point he became wildly delirious, and continued so for the next ten days, the temperature during this time varying between 101° and 103°. Respirations averaged 28 and pulse 120. During the following six days the temperature ranged between 99.5° and 101° and during the succeeding week, at the end of which he died, the temperature had again risen, varying irregularly between 99° and 103°, and without the pulse or respiration becoming altered appreciably. The day before he died the leukocytes numbered 23,200 (82 per cent. polymorphs), the red blood corpuscles 3,472,000, and the hemoglobin 60 per cent. Throughout his illness, aortic incompetence was diagnosticated, but no condition of pneumonia was determined. His chest, however, could not be fully examined, on account of his delirium, although it was noted that the chest was hyperresonant throughout on first examination, and toward the end there was a slight dulness at the lower part of the left side of the chest. At autopsy 50 c.c. of thin pus, from which pneumococc were isolated in pure culture, was found in the left pleura. The left lung was congested and edematous, but contained no pneumonic areas. The right pleura was universally adherent. The right lung was somewhat emphysematous, and showed a whitish firm area of chronic organized pneumonia, about $\frac{3}{4}$ inch in diameter, and a similar grayish, firm, non-friable patch, $1\frac{1}{2}$ by $2\frac{1}{2}$ inches toward the lower part of the upper lobe corresponding to the axillary region. There were also several small, firm, more reddish areas in the upper part of the lower lobe of the right lung. These, however, did not resemble infarcts in any stage nor any tuberculous or syphilitic process, and microscopically they were proved to be areas of organizing pneumonia in which the inflammatory exudate in the air alveoli were penetrated or even replaced by loops of granulation tissue extending from the alveolar walls.

Case X.—A large, well-nourished, plethoric-looking male, aged forty-three years. He had been an extremely heavy drinker, and gave a history of a sore on the penis, but no secondary symptoms. For several years he had been troubled with shortness of breath, but never had noted any edema. Three months previous to his entrance to hospital his friends informed him that he was jaundiced. Since

that time he emaciated rapidly and the jaundice deepened. Twenty-three days before admission, after he had been working around in a snow-storm, he had a severe chill, followed by high fever. Next day he felt catching pains in the right side of the chest, and became short of breath. He remained in this feverish condition until he came to hospital. On first examination there was noticed to be a moderate degree of jaundice, and the liver was readily palpable and slightly enlarged. The spleen extended $2\frac{1}{2}$ inches below the costal margin. The heart was dilated, and there was a soft systolic murmur best heard at the apex. The urine contained a considerable trace of albumin, and was passed in considerable quantity. The chest was barrel-shaped, and over the upper part of the right side there was a decided limitation of movement. In this situation over the upper and middle lobes, there was distinct dulness on percussion, and the breath sounds were high pitched and definitely bronchial. There were crepitations all over both lungs, much coarser over the right upper lobe. The temperature was 102.5°, respiration 36, pulse 126, blood pressure 135. The leukocytes were estimated at 40,000 per c.mm. (86 per cent. polymorphs); red blood corpuscles 4,248,000; hemoglobin 65 per cent. Six days later the jaundice remained the same, and the temperature continued irregulary raised to a maximum of 103.5°. The leukocytes were estimated at 35,000 per c.mm. (85 per cent. polymorphs), but two days later dropped to 26,800 per c.mm. He died in an extremely asthenic state fifteen days after his entrance to hospital, and on the fortieth day since the onset of his febrile symptoms. Until the end the temperature varied irregularly between 101° and 103.5°, and two days before death the leukocytes numbered 35,600 per c.mm. Dulness over the right upper and middle lobes persisted to the end, but the breath sounds over this area became rather fainter. During the last three days some dulness became evident over the left upper lobe, and during the last week ascites had developed, and rapidly increased. The presence of peritonitis was unsuspected, as he complained of no pain, nor was his abdomen specially rigid.

At autopsy the peritoneal cavity was found to be filled with a large amount of turbid fluid, which on microscopic examination was observed to contain numerous pus cells and pneumococci. The liver was in a condition of fatty coarse cirrhosis. The pleura on the left side was completely obliterated by adhesions, and the middle lobe and lower part of the upper lobe were involved in a process of organizing pneumonia, being dark reddish gray in color and fleshy in consistance. The upper lobe of the left lung was congested and slightly collapsed apparently by the action of the heart being pressed upward against it by the collection of fluid in the abdomen. It also presented quite a different appearance from the pneumonic condition in the right lung.

In such debilitated states as is illustrated by these cases, it is natural to assume a defective absorption of the exudate from the inflamed alveoli, and of course the patency and absorptive power of the lymphatics, as Koster suggests, is also naturally of the first importance.

As regards the miminum time necessary to produce a chronic pneumonia from the acute process, Ziegler places it at ten weeks, McCrea[27] at twenty-two days, and von Kahlden considered that any case persisting after fourteen days to five weeks would show organizing processes. In several cases which I have seen, where the pneumonic process seemed clinically to last as long as thirteen to fifteen days, the lungs at autopsy showed a condition of gray hepatization, but no organization. Fourteen days is possibly rather a low limit. In the ten cases here recorded the shortest duration was twenty-three days, but as was evident from the clinical histories, exact durations are in many cases impossible to determine.

The question of the type of the exudate into the air alveoli has also to be considered in relation to the occurrence of delayed resolution by organization. For instance, in pneumonia the exudate may be specially fibrinous, or it may contain an unusual number of leukocytes. Is this delayed resolution process then due to a defective emigration of leukocytes which do not remove the foreign material in the air spaces, as is usual by their vital action of phagocytosis, enzyme secretion, and solution, or is it, as Flexner[28] concluded, due to defective cellular content in the exudate and consequent failure of the autolytic processes of enzyme formation and fibrin solution which are known to follow on the death of cells and so necessitate the development of processes of organization? In relation to this latter view, however, if one might judge from the numerous evidences of cellular activity in pneumonia, resolution is more of the nature of a vital process and the removal of the exudate is by phagocytosis and active enzyme secretion, and is finally completed by absorption into the lymphatics of the alveolar walls.

In the present series of cases of delayed resolution pneumonia no special type of cellular exudate could be determined, chiefly from the difficulty of correctly reconstructing the process on account of the advanced age of the disease. The exudate into which the granulation tissue penetrated, consisted chiefly of rather small mononuclear cells, loosely aggregated, and generally surrounded by some loose fibrinous debris. Occasionally these mononuclear cells were relatively very large, and contained some blood pigment, but hemorrhages into the air alveoli were not particularly common. Plasma cells, as might be expected, were sometimes to be seen, but polymorphonuclear leukocytes were distinctly rare.

It is quite probable that there is a failure of leukocyte emigration or activity, and consequent defective bacterial destruction and

solution of the inflammatory exudate, or an insufficient proliferation or phagocytic activity of the lining cells of the air alveoli. Yet this was by no means easy to substantiate in these cases. It has, moreover, to be remembered that in most of the cases a continuous temperature, more or less, prevailed, and thus one might presuppose a continued infection of the air alveoli, and eventually as a necessary consequence the replacement of the renewed inflammatory exudate by organization.

The source of the indurating tissue in the lung in these cases has provided some considerable speculation. Ackermann and Thier-

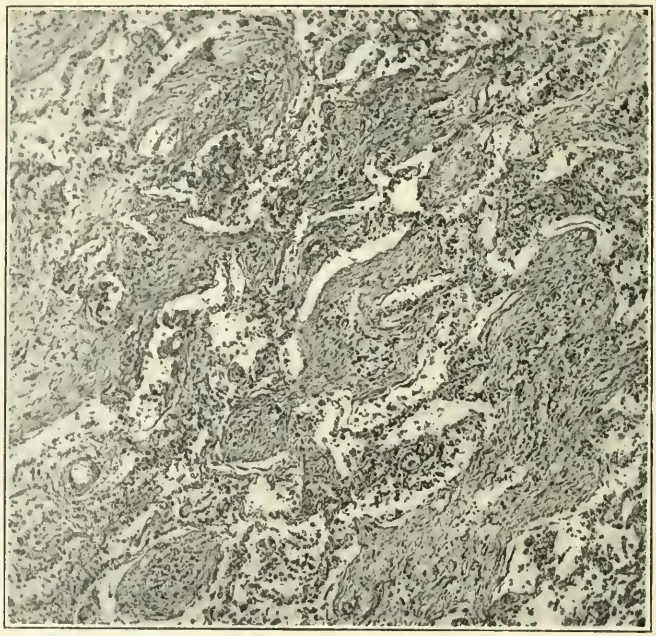

Fig. 1.—Case IV. Organizing pneumonia. The majority of the air spaces are almost completely filled with masses of fibrous tissue. × 65.

felder have considered the ingrowth of fibrous tissue into the alveoli as derived from the interlobular septa, and Eppinger and Cohn have advocated an extension from the peribronchial tissues as the essential factor in the induration. Heschl (1856), Woronochin (1868), Marchand (1880), Lindemann (1888), Cox[31] (1889), Rieder[32] (1890), Borrmann (1896), v. Kahlden (1987), etc., have all shown the origin of the new granulation tissue from the alveolar walls themselves.

In all the cases the process seemed to be much the same. The affected portion of the lung was practically airless, fleshy in consistence and in color, with the exception of two cases, where

it had a pale grayish-pink appearance. The overlying pleura was not specially thickened, nor was there any evidence of gross cicatrization in the pneumonic areas. On microscopic examination there was originally in all, apparently, an acute pneumonic exudate, which, in varying degree, was being organized by projection of granulation tissue from the alveolar walls, into the inflammatory exudate (Figs. 1 and 2). Some of the infundibular spaces and bronchi underwent a similar organizing process (Fig. 3), yet obviously this was not the initial condition. The air spaces were, as a whole, not particularly emphysematous, and the outlines of the alveoli, even although the whole air space was filled by organizing tissue, could still be, as a rule, easily

FIG. 2.—Air alveolus, showing organization of its inflammatory content. × 185.

determined, and did not appear disintegrated. The capillaries in the alveolar walls were generally somewhat congested, but stasis was not a marked or constant feature. The elastic-tissue structures of the alveolar walls were sometimes fibrillated, as is found in any case of pneumonia, and often irregular degenerated fragments of this elastic tissue could be seen among the granulations penetrating into the air spaces. No new formation of elastic tissue was found in the invading organization tissue in any case. For the most part the organization of each lobule was an individual process, yet frequently also an extension through from the adjacent lobules were observed. Organization usually took place as a projection from one or only a few foci on the alveolar walls. The extent of this

organization, of course, varied in the different cases, as in some the greater number of inflamed alveoli were penetrated and filled to a greater or less extent with the new fibrous tissue, and in others relatively few of the alveoli were involved in the organizing process. In one case, VIII, there apparently had been a more severe infection, and consequently a greater destruction of lung tissue, as in may places the sprouts of granulation tissue had become confluent (Fig. 4).

Tubercle bacilli and spirochetes were searched for in all the cases, but in none of them were any discovered.

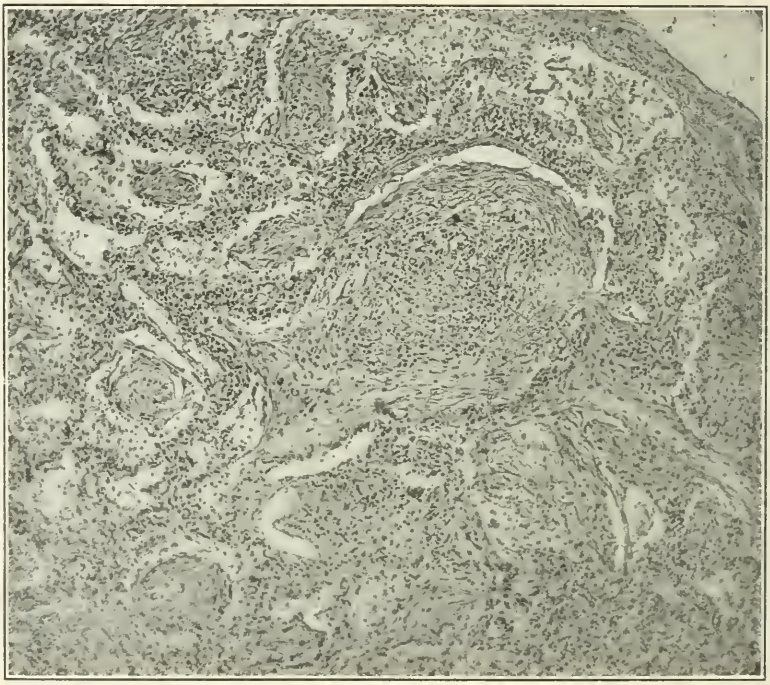

FIG. 3.—Case IX. Chronic pneumonia. Organization of inflammatory content in the ria alveoli and small bronchioles. · 100.

A great variety of conditions, of course, lead to induration of the lung, such as tuberculosis, pneumokoniosis, cicatrization around gangrenous areas or abscesses, but none of these closely simulate this condition of chronic organizing pneumonia.

Extension of fibrous tissue from the pleura is not a definite process, although the pleura is naturally a source from which scar tissue may be derived in the process of repair of damaged areas in the lung. Pleurisy itself does not usually extend its inflammatory process far into the lung (Fig. 5), and if any extensive fibrosis

in the lung is in connection with the pleura, it means the result of some irritative destructive or pneumonic process in the lung itself.

Cyanotic induration also has never the appearance of an organizing pneumonia either grossly or microscopically (Fig. 6).

Atelectasis of the lung, however, has grossly, in some cases, a close resemblance to the "carnified" appearance of an organized pneumonia. In collapse, however, the marked shrinking in volume, with the consequent aggregation of bronchi and vessels, provides some little distinction. A microscopic examination of 26 cases of

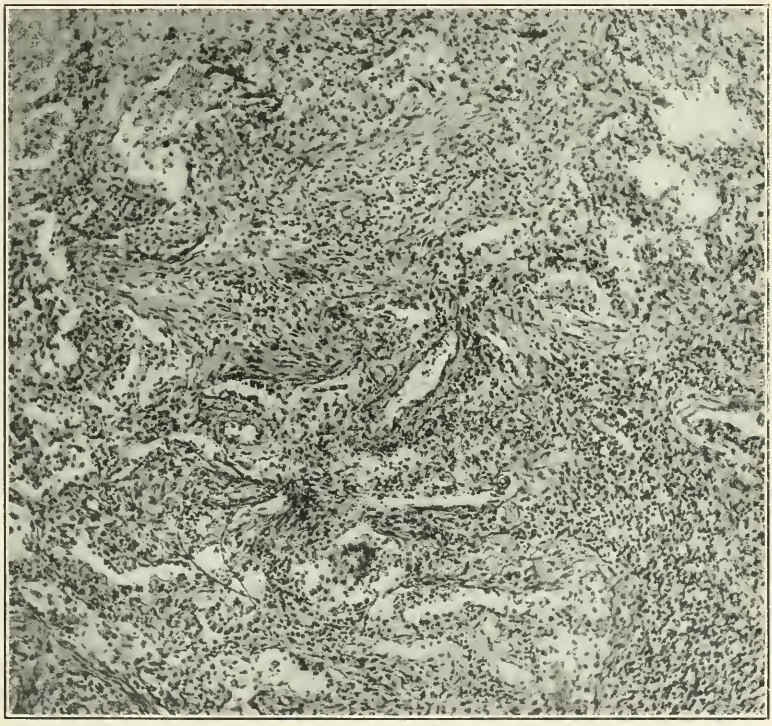

FIG. 4.—Case VIII. Organizing pneumonia. The air alveoli are extensively invaded by granulation tissue, but in many parts the walls are destroyed. In certain parts small abscesses are also evident. × 100.

old-standing collapse, resulting from the pressure of fluid in the pleural cavity, emphasized the distinction between this condition and pneumonic processes. To produce a complete collapse it requires a large amount of fluid exerting its pressure for some considerable time. The air alveoli may become so compressed that the walls may actually come in contact with each other, so that the whole tissue comes to resemble a mass of capillaries (Fig. 7). Usually, however, the lining cells become swollen, and thus what at first sight looks like a solid fibrous tissue is found to be a mass of

capillaries, including small collections of darkly staining small mononuclear cells, which once constituted the flattened lining epithelium of the air alveoli (Fig. 8). The interalveolar septa do become thickened, but on close examination it is surprising how little real fibrous overgrowth has occurred. Several authorities, however, such as Feustell,[33] have considered that in collapse there is an extensive fibroid development and Berlin[34] thought that even bronchiectasis might be produced by collapse and cyanotic induration. In some cases of old-standing collapse the quantity of

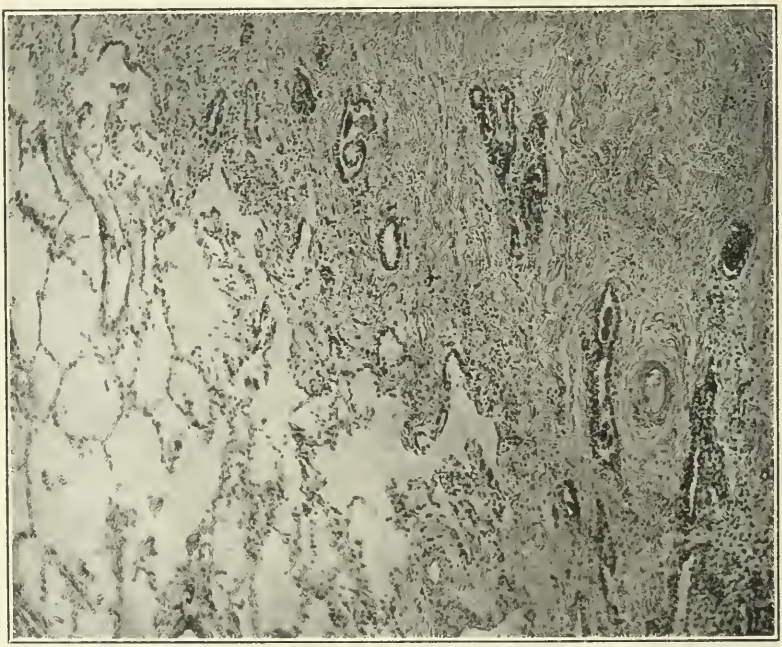

FIG. 5.—Chronic pleurisy, showing extension of chronic inflammatory tissue into the lung from the pleura. The lining epithelium of the air spaces included in the fibrous tissue has become swollen and adenomatous in appearance. × 100.

elastic tissue is apparently enormous (Fig. 9); yet on reconstructing this it is found that it is merely the normal alveolar elastic fibrils aggregated, fibrillated, and swollen up. A distinction between collapse and organized pneumonia had to be made in Case V, where there was about a liter of pus in the left pleural cavity. All the evidences, however, in this case—clinical, anatomical, and histological—determined in favor of a pneumonia. These conditions of organizing pneumonia, which are naturally associated with considerable congestion of the lung, may also occasion an effusion of fluid into the pleura, and thus again, unless carefully distinguished, become confused with collapse. Another example

may be noted where a mistaken autopsy finding was corrected microscopically, and by the clinical history. It occurred in a man, aged thirty-eight years, who had come to hospital for symptoms of cardiac failure, secondary to aortic incompetence. He developed signs of fluid in the right pleural cavity twenty days before death, but his temperature and respiration remained unchanged. Four days before death a typical lobar pneumonia of the right upper lobe set in, and the temperature rose to 103.8°, and remained about that level until just before death, when it fell to 97.2°. His leuko-

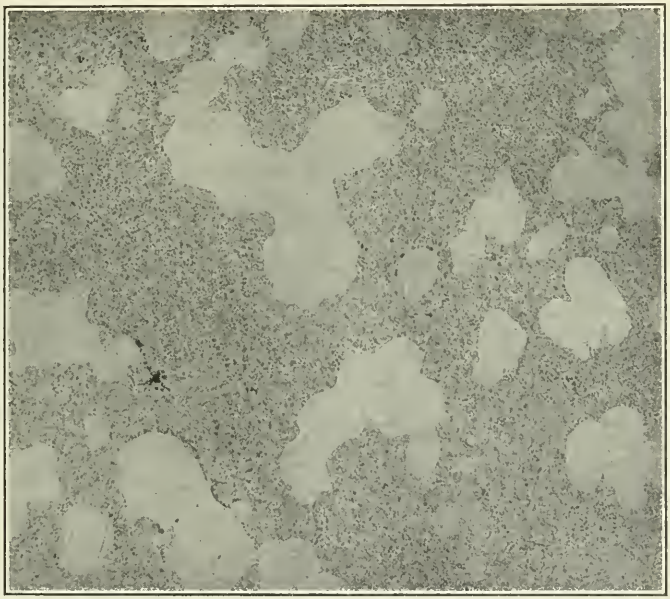

FIG. 6.—Cyanotic induration of the ung from a case of mitral stenosis in a boy. The interalveolar tissues are extensively thickened and infiltrated by new connective tissue. These thickened septa, however, contain congested vessels whose walls are thickened and some small alveoli completely filled with catarrhal cells and blood. The air spaces are occasionally filled with an edematous fluid or blood, but many are empty and lined with a flattened epithelium. There is no noticeable organization of the contents of the alveoli. × 75.

cyte count rose from normal to 20,000 (96 per cent. polymorphs), respirations changed from 23 to 44, and the pulse rate from 72 to 128.

At autopsy there was some thin, turbid pneumococci containing serous fluid in the right pleural cavity. The upper lobe of the lung was completely consolidated, showing a beginning gray hepatization. The lower lobe, particularly in its lower two-thirds, was dark brown, and fleshy in appearance. There was some considerable reduction in size, yet it seemed like an organizing pneumonia. This impression was, however, corrected on microscopic examination, as the usual

features of a collapse were demonstrated without any of the appearances of an organization of an inflammatory exudate.

Another case in which a mistaken diagnosis of organized pneumonia was made at autopsy was also of some interest. It occurred in an emaciated female, aged seventy years, who had died from asthenia consequent to a cancer of the head of the pancreas. There were numerous metastases along the lesser curvature of the stomach, involving both suprarenals, around the neck of the gall-bladder, in the liver, and in the retroperitoneal mesenteric mediastinal and bronchial glands. No metastatic involvement of the lung

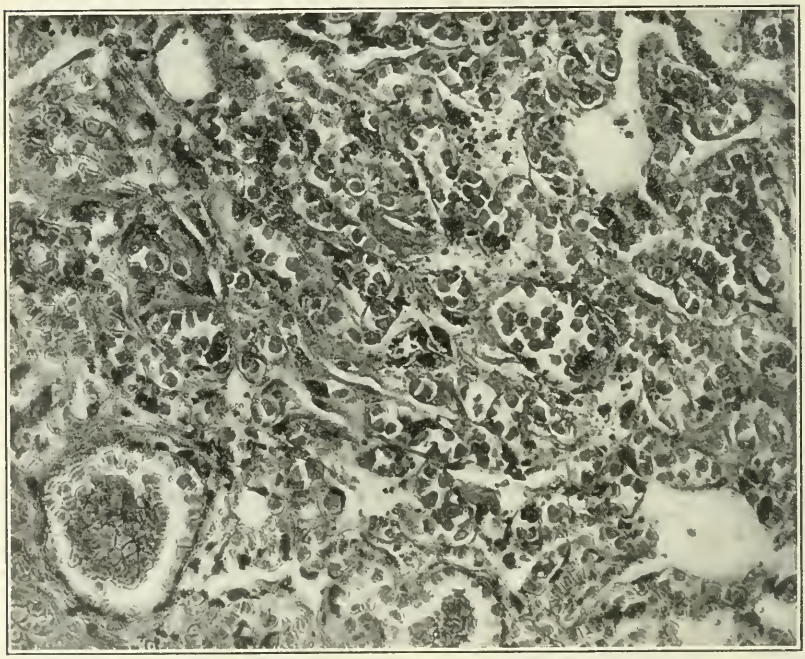

FIG. 7.—Collapse of lung, following pleurisy, with effusion. The alveolar wall capillaries are distended and crowded together. × 400.

was evident grossly. The middle lobe of the right lung, and also for a short distance above and below this, appeared firm, dark brown red in color, and traversed by a few fine, irregular, fibrous-looking streaks. This was considered to be an organizing pneumonia, but on microscopic section it was found to be a very diffuse cancerous invasion. Considerable portions of the lung tissue were exclusively occupied by the newgrowth, and in many parts also the air alveoli appeared filled with tumor cells. These alveoli, which were not invaded by cancer cells, were filled with an inflammatory content, nd there was also considerable inflammatory reaction in those into which the cancer elements had penetrated.

The other condition which presents features closely resembling chronic pneumonia, and with which in the past many cases have been classified, is the effect of syphilis on the lung.

At the present time, in spite of the great prevalence of syphilis and of syphilitic processes in other organs, lesions produced by it in the lung are of comparatively rare occurrence. An extensive literature has accumulated, as in older literature, syphilis of the lung occupied a much wider sphere and more important clinical interest.

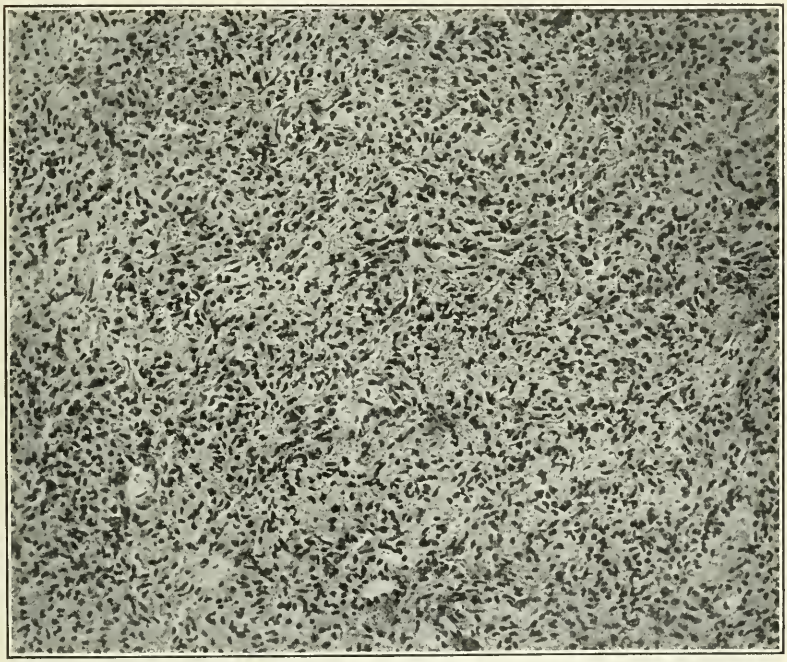

FIG. 8.—Collapse of lung, following pleurisy, with effusion. At first sight this tissue appears almost wholly fibrous, but on high-power examination the outlines of the alveoli can readily be determined. The alveoli are crushed together and their lining cells are swollen, giving thus the cellular appearance to the section. × 150.

Such authors on pulmonary syphilis, such as Peter Pinctor (1499), Paraselcus (1491-1541), Cesalpini (1601), Boerhaave (1668-1738), and Astruc (1684-1766), did not combine with the term "syphilis of the lung" any description of a specific lung disease, but only observed that following luetic disease there was a disposition toward phthisis. From the descriptions of Depaul in 1853 and then of Hecker, Ricord, Dietrich, and especially Virchow,[35] syphilis of the lung has become recognized, as in other organs, as a definite anatomical process. Wagner,[36] Calomiatti,[37] Carlier,[38] Hiller,[39] Heller,[40] and many others have described apparent syphilitic involve-

ment of the lung. More recently, however, as syphilis of the lung has become more thoroughly understood and differentiated, there have been comparatively few works on the subject. Among these latter, perhaps the most comprehensive are by Flockman,[41] Herxheimer,[42] and Brandenberg.[43]

The following two cases, although illustrating only one type of syphilis of the lung, are of some interest in affording a basis of comparison and contrast with the organizing processes following acute pneumonia:

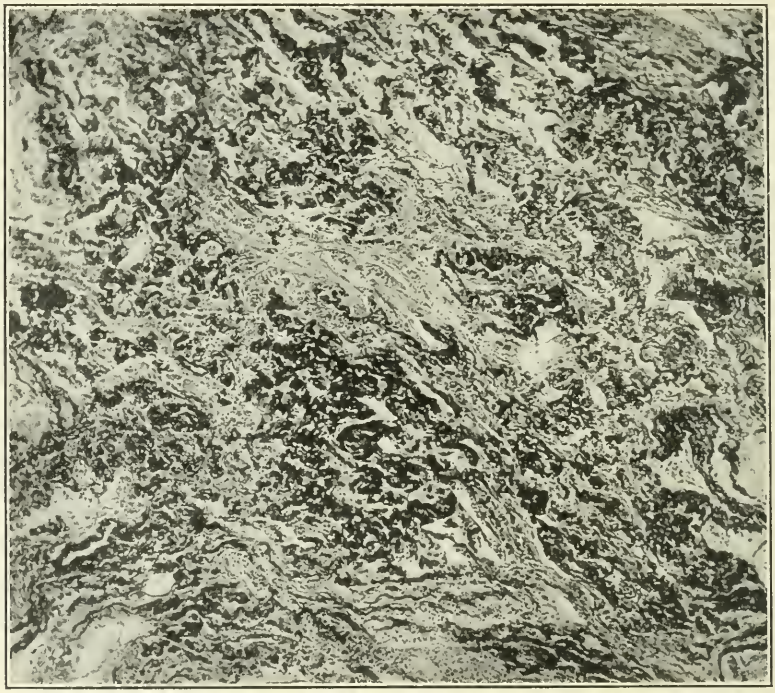

FIG. 9.—Collapse of lung, following pleurisy, with effusion. This is stained by Weigert resorcin-fuchsin method, and shows the apparently enormous amount of elastic tissue in such conditions. × 100.

Case I occurred in a fairly well nourished man, aged seventy-seven years, who had died from chronic nephritis and cardiac failure. The condition of his lungs during life had not disclosed any signs which had given rise to a suspicion of syphilitic fibrosis. At the autopsy no scarring of the skin, glandular enlargement, or other superficial signs indicated syphilis. Both pleural cavities contained a small amount of blood-stained serous fluid, and numerous stringy adhesions attached the lung to the chest wall posteriorly and laterally on both sides. The lungs were very emphysematous and anteriorly completely overlapped the heart. Over the lower lobes

the pleura was considerably thickened, and throughout both lower lobes, but particularly toward their bases, was a thick network of dense, well-defined fibrous tissue. There were no gummatous nodes, nor were there any large areas of fibrosis, although the strands of fibrous tissue varied considerably in thickness. Microscopically the fibrous tissue bands were fairly well defined, and were formed of old, dense, fibrous tissue. At the margins of this scar tissue there were, in places, small collections of anthracotic pigment, and in its interior remnants of included air alveoli were occasionally to be observed. The fibrous overgrowth was not particularly vascular, and its vessles were well formed and showed no perivascular lymphocytosis or obliterative endarteritis. There was no acute pneumonic or organizing process in the adjacent air spaces, and only a moderate degree of chronic venous congestion. No histological evidences of tubercle and no tubercle bacilli were to be observed. Spirochetes also, after repeated efforts, could not be demonstrated. There was some slight atrophic bronchitis, and the bronchial glands were small and atrophic. The larynx and tongue showed no particular change. The other organs presented no definitely syphilitic lesion. There was extensive general arteriosclerosis and considerable arteriosclerotic atrophy of the kidneys. The heart (650 grams) was dilated, and the myocardium of the left ventricle markedly hypertrophied, and the aortic valve segments sclerotic and incompetent.

Case II occurred in a somewhat emaciated woman, aged forty-four years, who had come under observation for constant headache which she had complained of for seven years and for pain and weakness of the legs during the last year. She presented the usual signs of tabes dorsalis, such as absence of the knee jerks, loss of pupillary light reaction, and optic atrophy. Her memory had lately become much impaired, and she was supposed also to have commencing general paresis. She had three children, all of whom died in infancy, but there was no history of miscarriages. She did not remember to have suffered from any previous illnesses, and denied venereal disease. She admitted, however, to have been in the habit of drinking five or six whiskys a day for the past fifteeen years. During the entire two months she was in hospital her temperature was somewhat irregular, every fortnight or so rising up to between 102° and 103.5°, and coming down by lysis in about six or seven days. For the last six days there had been another rise, but only to 100°, between which and 98° it varied until the time of death. There had, however, throughout been a slight cystitis, bacteria, and pus cells being passed in the urine. The urine, as a rule, was alkaline, of low specific gravity, and contained always a small amount of albumin and some granular, hyaline, and epithelial casts, and occasionally, expecially latterly, some blood. The thorax was symmetrical, large, and expansion fair. There was apparently no

abnormality on percussion, beyond some slight indefinite dulness at both bases; the vocal fremitus was noted as unimpaired. The breath sounds posteriorly were particularly feeble, and there were generally a few subcrepitant rales at both bases. The heart's apex was not palpable, but the outline of the heart was somewhat enlarged. There was a soft, systolic aortic murmur, which, however, was not transmitted far into the neck. The second aortic sound was markedly accentuated. Ten days before death she had an epileptiform convulsion and began to complain of severe headache, and since then was dull and irritable. Six days before death, coincident with a slight rise of temperature to 100°, she developed a cough, and there appeared an area of dulness over the upper part of the right lung, evidently from pneumonic consolidation. During the last two days of life she had almost continuous convulsions. The skin was dry and the bowels obstinately constipated. Pericarditic friction also developed at this time. Death apparently occurred from uremia.

At autopsy a considerable depression of the bridge of the nose, and numerous white, rounded scars, surrounded by a zone of brown pigmentation on the legs and abdomen, were observed. There was a large oval scar on the forehead the size of a silver dollar, and a large granulating ulcer discharging pus was situated on the upper part of the right thigh, but this did not apparently extend deeper than the subcutaneous tissue. Some of the scars were probably due to pediculosis, yet the majority were definitely of syphilitic origin. No general lymphatic glandular enlargement was noticeable. There was no fluid in either pleural cavity, and both lungs were densely adherent to the chest wall and to the pericardium. The lungs were somewhat emphysematous, completely covering the heart anteriorly.

The left lung on section, as a whole, was emphysematous and congested. In the lower lobe there was a dense network of fibrous tissue, particularly condensed at the lower anterior portion. About one inch from the lower outer margin was a large white cicatrix extending into the lung from the pleura for a considerable distance, and several other smaller scars also extending into the lung in other positions in the lower lobe. In the upper part of the lower lobe the fibrous network was more delicate and slightly pigmented. In the upper lobe there was practically no fibrosis. In the lower lobe between the meshes of fibrous tissue, and extensively in the upper lobe, were numerous large, friable, granular-looking areas of apparently gray hepatization pneumonia. Toward the apex these pneumonic areas were more or less confluent. In the lower lobe about the centre there was a circular abscess, about one-half inch in diameter, with rather ill-defined outline, and surrounded by a narrow congested zone.

The right lung was somewhat similar, a dense, fibrous network

pervading the lower lobe, particularly in its extreme lower part (Fig. 10). About the centre of the outer and extreme lower part of the lung there was a square-shaped area, about two inches in transverse diameter and one inch vertically, composed almost completely of dense fibrous tissue, and just above this a long, thick, fibrous scar extended for a considerable distance from the pleura into the interior of the lung. The upper and middle lobes were comparatively free from this fibrosis. As in the left lung, there were numerous acute bronchopneumonic patches, which in the upper part of the upper lobe were confluent. Several small acute abscesses were found in the interior of the lower lobe in its upper and middle portions.

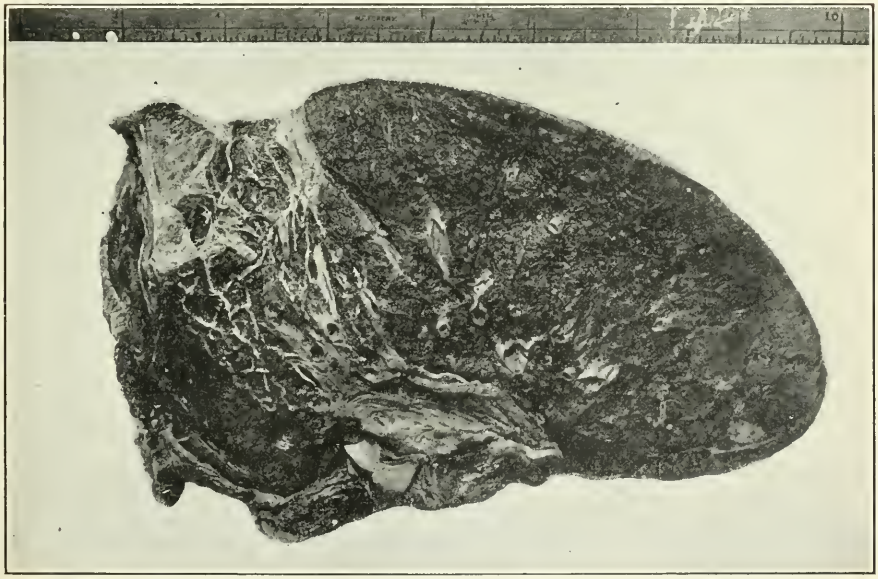

Fig. 10.—Syphilis of lung. Lower lobe extensively infiltrated by syphilitic cicatricial tissue.

Microscopically, the fibrous meshwork in the lungs was found to be composed chiefly of dense fibrous tissue. This fibrous tissue, however, varied considerably in age, as certain parts of it were of much more recent development than others. The fibrous tissue strands were not, as a rule, sharply defined, but extended irregularly among the lung tissue. The older portions were fairly vascular, and the capillaries were well formed as a rule. Many of these capillaries were surrounded by an extensive zone of lymphocyte aggregation, and in fairly frequent places inflammatory endarteritic processes, and even complete vascular obliteration, could be seen (Fig. 11). Remnants of included alveoli were common in the fibrous tissue, and they appeared as irregular, elongated,

duct-like acini, or merely as a small collection of darkly staining, small, somewhat cubical-shaped cells (Fig. 12). In the older portions of fibrous tissue there was a considerable representation of elastic tissue, existing in fine wavy threads. In the more recent parts the normal elastic tissue elements had apparently been more or less destroyed. At the margins of these fibrous trabeculæ the lung tissue for some distance outward showed a condition of organizing pneumonia (Fig. 13). This organization had occurred in much the same way as in the cases of organizing following acute pneumonia. Evidently in these places the inflammatory process had

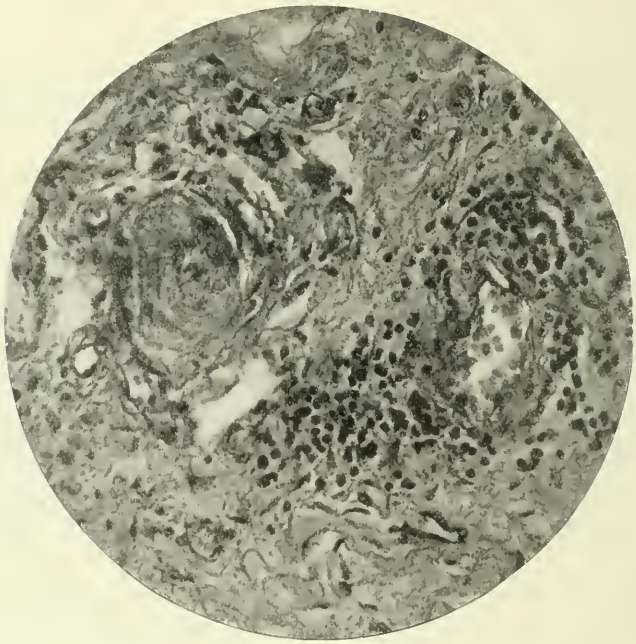

Fig. 11.—Syphilis of lung. Section from a fibroid area, showing one vessel surrounded by lymphocytes and snother almost completely obliterated by endarteritis. × 300.

not led to destruction of the lung structure, and the inflammatory exudate into the alveoli was being removed and replaced by the process of organization. In some places this organizing process was more extensive and more confluent, as some of the air spaces evidently had in parts been destroyed. The acute pneumonic areas seen grossly were in a state of gray hepatization, and they included numerous small foci of abscess formation. In no part of the lung, and after repeated search in a large number of situations, could either tubercle bacilli or spirochetes be discovered. Pneumococci and some staphylococci were commonly present in the gray hepatization areas.

The bronchial glands were slightly enlarged and pigmented, but showed no fibrous or tuberculous change. The bronchi were considerably congested, and their mucosa atrophied from chronic bronchitis. The larynx and epiglottis presented no abnormality except some congestion, and there was no smooth atrophy of the base of the tongue. Indeed, the papillæ at the base of the tongue were slightly hypertrophied.

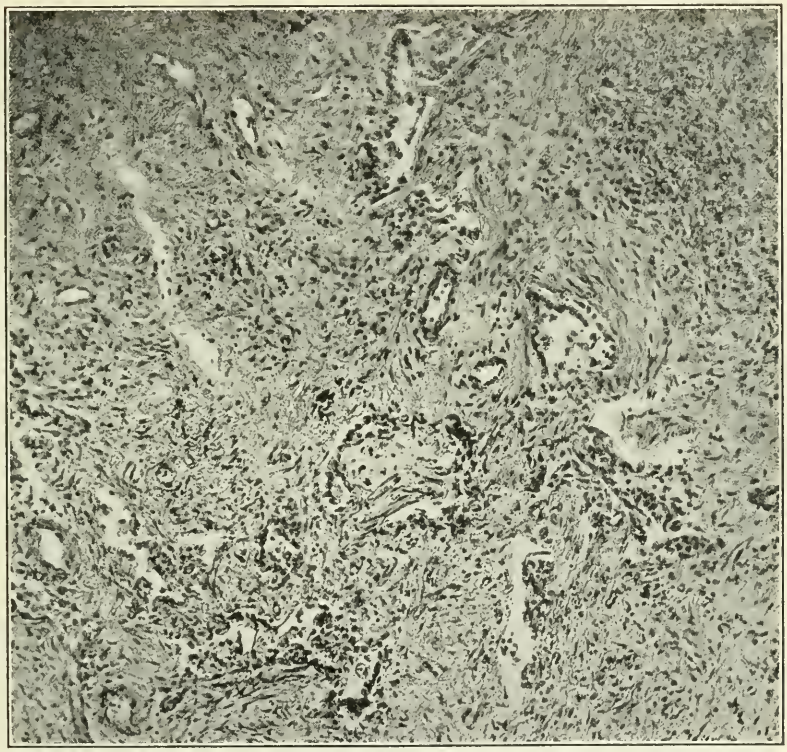

FIG. 12—Syphilis of lung. Dense fibrous area, including remnants of excluded partly destroyed air alveoli. × 140.

The pericardial sac contained about six ounces of a clear, blood-stained fluid. There were a few old adhesions at the base, around the origin of the great vessels, and the entire surface of the pericardium was covered by a shaggy fibrinous exudate. No organisms, tuberculous or otherwise, were found in this exudate, and considering the possibility of this inflammation being syphilitic, spirochetes were searched for, but could not be demonstrated. It appeared to be one of those cases of pericarditis which are found fairly frequently in association with nephritis.

The heart (550 grams) showed no special change beyond dilatation and some hypertrophy of the myocardium of both ventricles,

particularly the left. The aortic valves, the aorta, and coronary arteries, were only moderately atheromatous. The kidneys presented the usual appearances of advanced chronic nephritis. The liver (1500 grams) showed a deep typically syphilitic scar on its anterior upper surface, and microscopically it was found that the portal space fibrous tissues were considerably thickened, and contained dense aggregations of lymphocytes. No endarteritis, however, could be determined in the hepatic vessels.

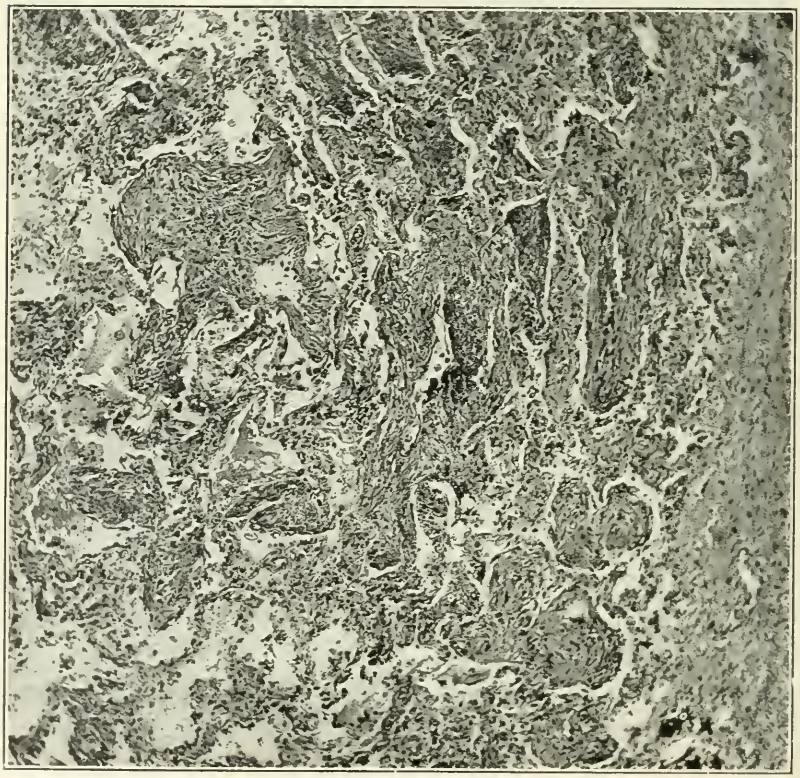

FIG. 13.—Syphilis of lung. Organization of the inflammatory contents of air alveoli. × 110.

The intestines showed no particular change, except the rectum which was stenosed by a ring of dense fibrous tissue about two inches above the anus. There was no ulceration around the constriction, and no glandular enlargement in relation to it. Microscopically, it was composed of dense fibrous tissue, and contained no evidences of tuberculosis. The mesenteric glands were not specially enlarged.

The meninges of the brain at the vertex were slightly thickened, and in patches adherent. The vessels at the base were extensively atheromatous, and there was considerable atrophy of the frontal

convolutions, as in early general paralysis. The interior of the brain only showed extreme edema without any gross lesion.

The spinal cord showed the usual degeneration of the posterior columns characteristic of tabes dorsalis.

These two cases then are examples of one of the varieties of syphilitic involvement of the lung.

Case I occurred in a subject who presented no other manifestations of syphilis in any other situation, and the pulmonary fibrosis was evidently of a very chronic, completely healed type. In the second case the process was much more recent, more widespread, and its relation to syphilis more definite from the numerous coexisting syphilitic lesions, as well as the suggestive vascular and other peculiarities in the fibrous tissue overgrowth in the lungs themselves. Both cases also conformed to the type generally described as diffuse interstitial syphilitic fibrosis as distinguished from the gummatous variety and the white pneumonia which is particularly found in congenital syphilis.

Diffuse syphilitic fibrosis has been considered by Pancritius to extend outward from the hilus, and Goodhart[44] advocated an extension from the pleura. In Greenfield's case, however, the pleura was free. Heller believed it to be a proliferation of the interlobular and interalveolar connective tissue, and partly from the vessel adventitia and Storch considered the process of diffuse syphilitic fibrosis to be originally derived from isolated areas which, through thickening and consequent lymphangitis, spread and united into a diffuse induration. In Case I the indurative process had evidently already become chronic and quiescent, but in Case II the process was comparatively recent, and still more or less active. The effects produced seemed to be consequent on a destruction of lung tissue, the damaged, irritated, and inflammed areas becoming organized by scar tissue, and the appearances presented depending on the severity, duration, and extent of the destructive process.

In one of the cases there was some resemblance in places to organizing pneumonia as well as the superimposed complication of an ordinary terminal pneumonia, and in this connection it is rather interesting to note that many of the older authors, such as Pavlinoff,[45] Kopp,[46] Sokolowski,[47] etc., have described a condition of syphilitic bronchopneumonia. Virchow guardedly admitted the possibility, but was doubtful of any special characteristics, and Ruhemann[48] stated that in acquired syphilis, bronchopneumonia was not so definite an event as in the congenital cases, and if such a thing existed it could not be distinguished from any other bronchopneumonia. Orth[49] and Birch-Hirschfeld[50] held that any relationship between bronchopneumonia and syphilis was very doubtful, and it does not now enter into any modern classification of the varieties of pulmonary syphilis. Pneumonia, although not of the type mentioned in the older writings, and although generally very

localized and irregular, is, however, a condition to be considered in pulmonary syphilis, as before fibrosis can occur some irritation or destruction must exist with the resulting production of a pneumonic process.

The conception of "syphilitic phthisis," as described in the older writings, has also undergone a similar modification. The condition known then as "phthisis ex lue venerea" appeared to be relatively common, and even Virchow agreed that cavities might form to produce a syphilitic phthisis. As late as 1881 Pancritius[51] described "syphilitic phthisis" as one of the most frequent of all diseases, his conclusions, however, being based almost exclusively on clinical data. Sokolowsky (1883) also described this condition, but Hiller[52] (1884) denied absolutely any such process, and following the discovery of the etiology of tuberculosis, practically all the cases previously described as syphilitic phthisis have become recognized as obviously tuberculous. The lack of proper distinction between syphilitic and tuberculous affections of the lung still gives rise to some difficulty, but in the older works provided some of the most surprising clinical pictures. Stengel[53] quotes Brambilla's case of a supposedly tuberculous patient who was given the mercurial inunction intended for a syphilitic in the adjacent bed, and this was followed by the prompt recovery of his symptoms. Gummatous masses may occasionally break down and form small cavities, but the majority of such cavities as do exist in syphilitic lungs are undoubtedly bronchiectatic. Tripier and also Bériel,[54] although probably somewhat too emphatic, relate the majority of cases of bronchiectasis to a syphilitic basis.

Clinically, the distinction between syphilis and tubercle is frequently difficult. In the works of Senger[55] and Porter,[56] Schnitzler,[57] Schiffmacher,[58] Schech,[59] Zinn,[60] and others numerous points of distinction have been advocated. The sputum examination, the temperature, and the presence of other syphilitic lesions may be of some little help, but the location and character of the signs by physical examination is perhaps of more importance. Pancritius, from a study of 106 cases, and Grandidier,[61] from 20 cases, came to the conclusion that the chief differential diagnostic point lay in the predominating affection of the middle lobe of the right lung in syphilitic processes, and Cube,[62] Kaposi,[63] and Aufrecht,[64] and many others have concurred in this. Ruhemann in 90 cases found 52.2 per cent. in the right lung alone, 11.1 per cent. in the left lung alone, 36.7 per cent. in both lungs. The right middle lobe was affected in 42.2 per cent., upper lobes 20 per cent. (both 9.8 per cent., right 7.7 per cent., left 3 per cent.), both lower lobes 8.8 per cent.

These data, however, refer to all kinds of pulmonary syphilis. White pneumonia, from most descriptions, is most commonly in the upper lobes or in the right middle lobe, and diffuse interstitial

fibrosis is generally met with in the lower lobes. Although the preponderance of tuberculous affections of the lungs are centred in in the upper lobes, yet, as they are commonly found in all situations in the lung, the diagnosis by location between syphilis and tubercle is thus necessarily very uncertain.

Pathologically even there may be uncertainties of distinction, as was noted by Saalfeld,[65] Ramdohr,[66] etc., between syphilis and tubercle, and Herxheimer (1907) observed that in some few cases the two processes were quite indistinguishable. As a rule, however, tuberculous conditions leave some definite characteristic traces both in gross and microscopic examination. The presence of giant cells is no absolute criterion of tubercle, as they have also been noted in syphilitic processes, particularly in relation to gummas, by Baumgarten,[67] Brodowsky,[68] Hansemann,[69] Brandenberg, etc. The finding of tubercle bacilli is of course positive of tuberculosis, yet if not discoverable it does not contraindicate tubercle, as the organisms are often particularly hard to demonstrate in many chronic, definitely tuberculous lesions. The demonstration of spirochetes has about the same relationship to syphilis, as they are only rarely found. Levaditi, Roche, Brandenburg and others have observed this, and also stated that in all the more chronic lesions of acquired syphilis they are relatively infrequently found. In the manifestations of congenital syphilis, however, they are, as a rule, much more frequently demonstrable. In neither of the two syphilitic cases detailed in this present communication could either spirochetes or tubercle bacilli be observed in any situation.

As indicative of syphilitic lesions in the lung, the peculiar hyaline appearance of the connective tissue, the finding of gummas if present, the high degree of vascularization as compared with tuberculous processes, the perivascular lymphocyte aggregations (Fig. 11), and particularly the endovascular changes (Fig. 11), are important. These vascular changes have been observed, as in syphilitic conditions in other organs, in the lung by Birch-Hirschfeld, Greenfield,[70] Petersen,[71] Pavlinoff, Councilman,[72] Storch,[73] Brandenburg, etc. It has been suggested that the whole process of fibrosis depends on this vascular obstruction, but in considering the relatively small number of vessels involved this cannot be so.

There still remain to be considered those cases where tubercle and syphilis coexist. Rindfleisch (1894) described a case of mixed tuberculosis and syphilis. The subject was first tuberculous, and syphilis was subsequently acquired. After death both processes were distinct in the lung, the syphilitic nodules being encapsulated from the tuberculous foci. Borst[74] has referred to a combination of miliary tuberculosis, with syphilitic affections, the syphilitic process encapsulating the tubercles. Hansemann[75] takes the stand that most syphilitic conditions on the lung are apt to become secondly infected by tuberculosis. Out of 22 cases which he examined, in

only 5 were tuberculous lesions not demonstrable. Eppinger[76] and Potain[77] came to somewhat the same conclusion, but Flockmann and also Mauriac[78] have denied any more than an accidental association. Keyes[79] also has observed that the combination of syphilis and tubercle has been much overrated. Fournier[80] has stated that when syphilis was engrafted on a proved case of tuberculosis the course of the latter became more rapid and severe. Also when pulmonary tuberculosis became evident in the early stages of lues, there was a rapid extension of the tuberculous process, and the prognosis was very grave. When tuberculosis, however, was consequent to an old standing luetic infection the disease was apt to assume the form of a tardy sluggish afebrile type.

As far as these cases would seem to show, organizing pneumonia is a condition which generally can be fairly easily distinguished from a syphilitic process. There are not the same vascular changes, nor is there the same tendency to destruction, and the irregularity of the whole process in syphilis is also strikingly different.

Such conclusions as may be drawn from these 10 cases of chronic pneumonia are:

1. That they are a possible sequence of acute pneumonia.

2. That they are particularly found in subjects debilitated by some intercurrent condition, but that no single factor such as cardiac conditions, nephritis, arteriosclerosis, alcoholism, tuberculosis, or syphilis is responsible for its production.

3. The onset is extremely irregular in type, and may be acutely febrile, simulating the usual commencement of a croupous pneumonia in subjects of the same age (Cases IV, VII, IX, and X), or typical signs of pneumonic consolidation may be evident without there having been any especial initial pneumonic symptoms (Cases II, III, V, and VI), or there may even be no increase in temperature or abnormality of the pulse and respiration rates (Cases I and VIII).

4. The prognosis in such conditions is bad, as not only is death very frequent from cardiac insufficiency, but complications, such as empyema, pericarditis, peritonitis, meningitis, etc., are extremely frequent, and what is very important that any of these conditions may supervene even after long periods of apparent quiescence of the pneumonia—7 out of the 10 cases were complicated in this way, an infinitely higher proportion than occurred in the rest of the pneumonia series; 41 out of 95 cases of lobar pneumonia, including 9 which had become organized, and 10 out of 64 cases of bronchopneumonia, including 1 which was organized, were complicated.

5. Such conditions may undoubtedly be recovered from as far as symptoms are concerned, yet maintaining physical signs of pneumonic consolidation. It is just such cases which are apt to be mistaken for tuberculosis or possibly syphilitic fibrosis. In this

connection it is also possible that the development of bronchiectasis or subsequent tuberculous infection may further complicate the case.

6. Collapse, tubercle, infarcation, and syphilis of the lung, etc., are distinguishable from chronic pneumonia.

7. Once organization processes in the lung have advanced to any marked extent one cannot imagine any complete restoration, as some cicatrization must be permanent.

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REVIEWS

Differential Diagnosis. By Richard C. Cabot, M.D., Assistant Professor of Clinical Medicine, Harvard University Medical School, Boston. Pp. 753; 195 illustrations. Philadelphia and London: W. B. Saunders Company, 1911.

It is not to be denied that Dr. Cabot, more than anyone else in the United States, has been instrumental in devising new and improving old methods of teaching medicine. His latest book on differential diagnosis indicates no diminution of his originality, and whatever may be the opinions of his readers, and doubtless they will vary a good deal, no one can read it without being stimulated and aroused to perfect himself in the fundamental and most difficult department of medicine, diagnosis. Like all things, however, this book is not wholly new, but its evolution can be traced through a series of other works of greater or less importance. I do not mean to imply that Dr. Cabot has consciously copied. It is more than likely that he is not personally familiar with many of the books in which a somewhat similar attempt has been made, but these books, at least those of them that are really good, have influenced medical thought and medical literature, and it is altogether likely that without them Cabot's book would not have been possible. A pattern of such work was Richard Bright's *Reports of Medical Cases*. Although it is not strictly a work on differential diagnosis, nevertheless both Bright's and Cabot's books are constructed on essentially similar lines. Bright, it is true, groups his cases sometimes according to a morbid lesion, rather than according to subjective and objective symptoms. Hilton's work on *Rest and Pain* incidentally discusses a good deal of differential diagnosis, particularly in reference to subjective symptoms, and has also played its unconscious part. Another book now wholly forgotten is a work on *Practical Medicine*, edited by John M. Galt, published in 1843, in which the subject of medicine, classified largely according to important symptoms, is wholly illustrated by actual cases. Still another to which reference should be made is Pershing's *Diagnosis of Nervous and Mental Diseases*, in which the classification is wholly according to symptoms, an ambitious and reasonably successful attempt.

Dr. Cabot's book consists of a small amount of comment and 383 histories. These are all presented under four heads: (1) The history, clinical symptoms, physical signs, and laboratory reports;

(2) the discussion which involves more or less differential diagnosis; (3) the outcome; and (4) the final diagnosis. In addition, there are diagrams at the beginning of each chapter to show graphically the relative frequency of the various causes of the symptom under discussion. These diagrams are based partly on Dr. Cabot's own investigations, partly upon statistics obtained from the literature. There is also at the end of many of the articles a table of differential diagnosis. It is upon the case histories that the value of the work will ultimately depend. These are presented with the dogmatism so characteristic of Dr. Cabot and in language that not infrequently is unconventional, but which is always precise.

There will be many instances where the reader will disagree with Dr. Cabot, but this only adds to the interest of the book. Often Dr. Cabot states that a differential diagnosis between certain things is impossible, and fails to mention physical signs which might aid the differentiation. He is fond of speaking of wild and untamed physical signs, which, according to him, are signs absolutely in disagreement with the diagnosis, and therefore serve to indicate how carefully the case has been studied. I think that few will be willing to accept dynamic aorta as a final diagnosis. The important thing is that Dr. Cabot has produced a book on unconventional lines that is useful, and, more than its mere utility, is stimulating.

Regarding the diagrams, we cannot share his enthusiasm. Undoubtedly it is desirable to have numerical statements of clinical facts and such statements are of importance if they are true. The presentation of these diagrams, even if they are inaccurate, may serve to call attention to the necessity of gathering further statistics, and they are at least no worse than the hazy ideas upon the subject possessed by some of us. However, it is my impression that should this further study be undertaken, the appearance of some of the diagrams will be very radically changed. J. S.

Progressive Medicine. A Quarterly Digest of Advances, Discoveries, and Improvements in the Medical and Surgical Sciences. Edited by Hobart Amory Hare, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College. Assisted by Leighton F. Appleman, M.D., Instructor in Therapeutics in the Jefferson Medical College, Philadelphia. Volume I, pp. 355; 18 illustrations. Volume II, pp. 397; 51 illustrations. Philadelphia and New York: Lea & Febiger, 1911.

Volume I of *Progressive Medicine* begins with a discussion of the surgery of the head, neck, and thorax, by Charles H. Frazier.

After devoting 12 pages to the surgery of the face, jaw, mouth, and tongue, he deals with the neck, especial attention being given to tuberculous adenitis. Next follows a full account of various conditions of the thyroid, thymus, and parathyroid glands. The succeeding 28 pages are given over to a consideration of the surgery of the brain, especially tumors, and the cranial nerves, the latter being considered in great detail. In a like number of pages devoted to thoracic surgery, the more important recent advances dealing with the heart, lungs, pleura, and esophagus are taken up, together with a concluding section on the mammary gland. In an article of 132 pages, John Ruräh has furnished an excellent and complete summary of the work done during the last year in infectious diseases. After paying a graceful tribute to the memory of Robert Koch, he calls attention to the most notable therapeutic achievement of the year, the introduction of salvarsan by Ehrlich and Hata. A discussion of various general factors in the spread and production of disease is followed by a consideration of most of the infectious diseases, including those due to parasitic agents. Cholera receives full and timely recognition. Poliomyelitis, tuberculosis, and typhoid fever are accorded most thorough treatment. Floyd M. Crandall, in 31 pages, deals with certain phases of diseases of children. Infant mortality, hemorrhagic disease of the newborn, diseases of the urinary tract, are among the subjects discussed. In addition, 19 pages are devoted to the question of infant feeding and the stools and digestion in infancy. Dr. D. Braden Kyle's interesting contribution on Rhinology and Laryngology occupies 43 pages of the volume. He takes up important advances in our knowledge of the nose and the accessory sinus, the pharynx, larynx, and the tonsils. In the concluding 25 pages on otology, Arthur B. Duel discusses at some length deaf mutism, otitic meningitis, the Eustachian tube, sigmoid sinus thrombosis, the value of the Wassermann test in internal ear disease, and the use of vaccine therapy for purulent aural infections. As during each succeeding year the volumes of *Progressive Medicine* appear, the value of the work as a reliable guide to medical and surgical progress becomes more and more apparent. In this respect the first volume of 1911 is no exception to the many that have preceded it.

Two thirds of Volume II of *Progressive Medicine* deals with topics that are largely surgical. In the first 40 pages William B. Coley goes at length into the subject of hernia. The operative treatment, numerous unusual forms of hernia, and various complications of the condition are taken up. Arpad G. Gerster has furnished an admirable review of 96 pages on the surgery of the abdomen. He enters into the many important advances in abdominal diagnosis that have of late resulted from the use of Röntgen rays, and describes, among other interesting procedures, the use of Momburg's aortic tourniquet and a method

of draining ascites into the subcutaneous abdominal tissues. The omentum and stomach are considered; under the latter especial attention is paid to the surgery of gastroptosis, acute gastric dilatation, hemorrhage, and ulcer. A number of pages devoted to the intestines and appendix conclude his observations on the intestinal tract proper. Finally, he considers the liver and portal veins, the pancreas, and spleen. Under the latter heading, Banti's disease is fully discussed. It is of interest to note that the recent articles on the Cammidge reaction are unanimous in regarding the test as useless for the diagnosis of pancreatitis. The gynecological section of 104 pages, by John G. Clark, comprises 33 pages on the cancer problem in general and that of the uterus in particular. The remaining pages contain an excellent digest of a number of subjects of live interest, among which may be mentioned uterine fibroids, displacements and prolapse of the uterus, pelvic inflammatory diseases, the relationship between rectal and pelvic diseases, backache, and various phases of the menopause. The medical portion of the volume consists of Alfred Stengel's usual valuable contribution, which occupies 101 pages. Under the blood, he has entered fully into pernicious anemia, chlorosis, the leukemias and chloroma, hemophilia, purpura, and Addison's disease. Then follow discussions of myxedema and cretinism, Banti's disease, and splenomegaly. Several pages suffice for a review of what has been done of late on Hodgkin's disease and diabetes insipidus, whereas diabetes mellitus and exophthalmic goitre embrace the concluding third of his article. The final section of the volume contains 25 pages by Edward Jackson on ophthalmology. Before he takes up diseases of the several portions of the eye, as the conjunctiva, cornea, uveal tract, crystalline lens, retina, optic nerve, and lacrymal apparatus, he calls attention to the influence of salvarsan on the eye, and concludes by considering injuries to the eye. The entire volume is of exceptional interest, and its perusal will amply repay all who desire to familiarize themselves with the many important advances that have recently occurred in the branches of medicine and surgery which it covers. G. M. P.

Diagnostik der Nervenkrankheiten. Dr. L. E. Bregman, Oberarzt am städtischen jüdischen Krankenhaus in Warschau. Mit einem Geleitwort von Hofrat Prof. Dr. H. Obersteiner in Wien. Pp. 535; 193 illustrations. Berlin: S. Karger, 1911.

This is essentially a diagnosis for diseases of the nervous system. The plan of the work is excellent, but its uses will be limited because the work is not sufficiently extensive. Its plan is to present symptoms

and to mention all the possible diseases in which a given symptom may be present. For example, when discussing motor symptoms, those relative to the peripheral and cranial nerves are discussed, and then those relative to cerebral and spinal diseases, but there is no distinctive effort to cover the symptoms of any one disease unless it comes purely within the classification of motor, sensory, or special symptomatology. For example, while locomotor ataxia is considered in several places, the disease as a whole is not taken up, but when discussing aphasia the subject is comprehensively handled because it is considered as a distinct symptom. While this method has its advantages, its disadvantages are apparent.

From the standpoint of symptomatology it is perhaps the best presentation that the reviewer knows, for no symptoms has been neglected. The extent of the subject is comprehensive and neurologists will find most symptoms amply discussed, although by no means exhaustively.

It has the usual failing of most foreign text-books, articles, and monographs, that is, references to American authors are sadly lacking. Why this should be so in the present age of scientific medicine, especially considering the advances which have been made by American physicians, is difficult to understand. There is probably only one Continental neurologist who consistently mentions Americans—Oppenheim—and it is indeed with pleasure that American neurologists contemplate that he is probably the best that Europe has. Therefore, there is less reason for others to be provincial. However, the foreigner is not altogether at fault, for it is a notorious fact that American authors, not always neurologists, have a predilection for mentioning foreign authors and neglecting their own countrymen. This is not only true in scientific articles, but is also true in the abstract department of some American journals, for while the presumption is that a German journal, for example, is for the Germans, and then for others, a French journal for the French, and then for others, an American journal (supported by Americans) is first for the others, and then for Americans. This is only too true.

Specifically, it is difficult to criticise this book, and only certain subjects will be touched upon. The description of nerve palsies is excellent, but it is interesting to note that the author refers only in a footnote to the newer classification of deep, epicritic, and protophathic sensibility. In discussing the disturbance of sensation resulting from cortical lesions, he fails to refer to segmental disturbances, but this would be expected, inasmuch as Americans first called attention to it. In discussing the occurrence of the Babinski reflex in motor cortical lesions, he states that it is absent in many cases; but it has recently been pointed out, however, that this phenomenon is present only in cortical lesions limited to the leg centre. In discussing aphasia, he disposes of Marie's newer

ideas almost in a paragraph, and sticks to the older classifications. These, however, are only minor criticisms. The illustrations are fairly good, although it is difficult to understand why in most German books, whenever the author has an original picture, the words "Eigene Beobachtung" are always given in the legend, for the presumption is that if not otherwise indicated, the pictures are by the author. T. H. W.

Practical Treatment. A Handbook of Practical Treatment. In three volumes. Edited by John H. Musser, M.D., Professor of Clinical Medicine, University of Pennsylvania, and A. O. J. Kelly, M.D., Assistant Professor of Medicine, University of Pennsylvania. Volume I; pp. 909; 227 illustrations. Philadelphia and London: W. B. Saunders Company, 1911.

"There is in Medicine an art and a science, each mutually dependent on the other. The practising physician's chief concern, however, is with the art, rather than the science. . . ." With this as the opening sentence, the editors strike the keynote of the work before us. This expression, coming from the diagnostician, the consultant, the teacher, the laboratory expert, and the practising physician, each of whom is represented in one or the other or both of the two editors of this treatise, has an authoritative significance of considerable interest. Especially is this true to-day when the mutual dependence of the art and the science is coming to be recognized by the more thoughtful of those governing the direction of medical development.

The time is ripe for just such a book as this. The treatment of many diseases has, through experiment, passed either entirely out of empyricism, or theory and reasoning has led scientists far toward the solution of the body's defensive and offensive mechanism. *A Handbook of Practical Treatment*, therefore, written today by such international authorities as compose the list of 79 contributors to this work, constitutes an indispensable aid to the practitioner.

Among the contributors are surgeons and specialists in various branches of medicine. This is, as the editors rightly term it, an "innovation" by which "the treatment of certain borderland and other diseases" is discussed by "physician and surgeon" or specialist "so that the reader may have the benefit of the points of view of both."

The book is in marked contrast to former works on this subject, in that drugs and prescriptions constitute a very minor part.

Among comparatively new subjects in a work of this kind are the following: Preventive Treatment; General Principles of Dietetics, Serum Therapy, and Organotherapy; The Rest Cure, The Work Cure, and Psychotherapy; Exercise; Massage and Mechanotherapy;

Hydrotherpay and Balneotherapy; Climatotherapy and Health Resorts; Artificial Aërotherapy; Electrotherapy and Radiotherapy.

"Preventive Treatment" deals with National, State, and Municipal Health Boards. Under this head also appears "Prophylaxis of Infectious Disease," "Disinfection," and "Protective Inoculation," the latter being but briefly treated, as it is more fully dealt with under serum therapy.

To the subjects "General Principles of Dietetics" and "Dietetics of Infancy" is allotted 118 pages in this volume of 909 pages. Technical discussions of these subjects are omitted, but sufficiently detailed consideration of methods of determining food values for infant and adult is given to enable the practitioner to exercise his own judgment in making up dietaries. This is to be preferred to the usual custom of itemized meals for pathological conditions, often wholly unsuited to the patient in question.

The chapter on "General Principles of Serum Therapy" will be read with much interest. It is a thoroughly up-to-date authoritative discussion of this foremost subject in modern medicine. Protective and curative inoculations in certain disease conditions are considered. Possibly lack of space prevented, but it would have been helpful to the practitioner had a few temperature charts been introduced to show some of the reactions and their significance.

In the chapter on "Organotherapy" the writer takes a very gratifyingly conservative view of the subject which it is to be hoped will check the irrational therapeutist and medical faddist. The chapter on "Exercise, Massage, and Mechanotherapy" is probably the most comprehensive treatment of the subject that has as yet appeared—certainly in a handbook.

Hydrotherapy and Balneotherapy, recognized as essential to most modern hospitals, are thoroughly discussed and illustrated under this head.

The subject of Climatotherapy, usually briefly dealt with in text-books and too extensively treated of in special publications, is presented succinctly, with, however, specific reference to resorts and their suitability to different pathological conditions.

While, as already stated, the consideration of drugs, as such, receives little space in this volume, the subject of drug action is dealt with under the headings "The General Principles of Drug Treatment" and "Drug Poisoning and Drug Habit."

The index, a portion of these large works often recklessly neglected, is practical, thorough, and, so far as tested, accurate.

The book is possibly too bulky, and this is only the first volume. When, however, one considers the immense amount of material which may be comprised under the term "Treatment," the editors, by judicious omission, will be found to have done well in reducing the mass to even 909 pages. Long dissertations on drugs whose actions are imperfectly understood and on methods of doubtful merit are conspicuously absent.

As one reads, in review, the chapters which compose this volume, the impression is that here are the modern methods acceptable to authoritative and conservative medical men. Such a book must, therefore, be an essential in the equipment of the practising physician who would guard himself against the fallacies and errors which have brought treatment into such disrepute from time to time.

Lack of space prevents detailing further the many features of this work which deserve notice. One cannot, however, close this review without a word regarding Dr. A. O. J. Kelly, whose death has proved such a loss to American medicine. Conversant with the laboratory as well as the clinical side of medicine, he was eminently fitted to act, together with Professor John H. Musser, as the "guiding hand" in the production of this valuable addition to medical literature.

C. N. B. C.

Sehprobentafeln zur Bestimmung der Sehschärfe für die Ferne. Für die Zwecke der Praxis und mit besonder Berücksichtigung der Bedürfnisse der ärztlichen Gutachtertätigkeit. Test Objects for Determining the Visual Acuity for Distance. Intended for Practice and with Particular Consideration of the Requirements of Medical Certification. By Dr. v. Ammon, Army Surgeon and Oculist in Munich. Second edition; 8 lithographic tables. Munich: J. F. Lehmann, 1909.

The purpose of the designer of these test cards has been not simply to offer to the examiner test types and objects which might be in some respects an improvement upon the many existing ones, but his object has been to supply a method of testing central vision which shall be as far as possible objective in character and to permit ready comparison between and control of the statements of the person under examination by suitable variation of the methods of examination. Direct view of the test object, controlled by reflection of the same in a mirror, is one of the ingenious devices employed as follows: The subject is asked to read the lowest line he can decipher. He is then requested to read from an identical card (in reverse type) when reflected in a mirror. If the two agree the result may be accepted as the real degree of central vision. A simulator would be liable to select the same lines in each test, not knowing that the reflected letters can be so arranged that their virtual distance is greater than by the direct test, and thus require a higher degree of visual acuity. The cards also contain a number of other ingenious devices which fulfil a needed requirement not to be found in the usual armamentarium of the oculist.

T. B. S.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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The Etiology of Scarlet Fever.—S. Bernhardt (*Deutsch. med. Woch.*, 1911, xxxvii, 1062) referred in his first report to cell inclusions in scarlatina. The present note deals with these bodies. He found certain cellular inclusions resembling the trachoma bodies in the mesenteric lymph glands of three patients dying early in the course of scarlet fever and in the kidney cells of one case. Similar inclusions have been found in the lymph glands of apes infected with scarlet fever. On injecting these glands into other apes, a disease like scarlatina in man was produced. In the control material examined, such inclusions have not been found. P. A. Hoefer (*Ibid.*, 1911, xxxvii, 1063) also reports the finding of intracellular bodies in scarlatina. The bodies he describes are larger and differ from those of Bernhardt. Prof. Hartmann, who has seen the preparations of both Bernhardt and Hoefer, expresses the opinion that the findings of these two workers are not identical, but considers it possible that each may represent stages in the development of a parasite. Hoefer's inclusions were found in the cells of the spleen, lymph glands, and mucous membranes of fatal cases of scarlatina.

A Modification of the Acetic Acid Test for Albumin in the Urine.—Glaesgen (*Münch. med. Woch.*, 1911, lviii, 1123) calls attention to a method of employing the acetic acid test for the detection of albumin which has been used for years in France. Method: 20 c.c. of urine, about three-fourths of a test-tube 1.5 cm. in diameter, are treated with five drops of 20 per cent. acetic acid, mixed, and one-half poured into a second test-tube. The contents of one tube are boiled, the other

serving as a control. Albumin produces a cloud or precipitate in the boiled tube. Before testing, the urine must, of course, be perfectly clear; if necessary, shake it with Kieselguhr and filter. If the acetic acid causes a cloud in the cold (nucleo-albumin), it is cleared by filtration before boiling. With an alkaline urine, acidulate slightly to prevent the precipitation of the phosphates, or, if a precipitate of phosphates appears when the urine has been treated with acetic acid and boiled, a few more drops of the dilute (20 per cent.) acid may be added to dissolve it. This will not redissolve even a slight albuminous cloud, provided the urine is not boiled again. Glaesgen has compared the test performed in this way (1) with the usual method, *i. e.*, boiling the urine and then adding dilute acetic acid; (2) with the acetic acid and potassium ferrocyanide test; and (3) with Heller's test. He used urines with known albumin content and diluted them with urine which was negative to Spiegler's reagent. He found that the test as described would detect albumin in a dilution of about 1 to 180,000, the heat and acetic acid test in 1 to 130,000, acetic acid and potassium ferrocyanide, 1 to 70,000 after standing some time, and Heller's 1 to 35,000. In no case where physical examination of the patient did not reveal an adequate cause for a trace of albumin was the test positive. He therefore thinks it does not react to the minute quantity of albumin present in normal urine. When a patient is on a milk diet, the urine may be so poor in salts that a trace of albumin may be missed with this test. But the addition of sodium chloride obviates this difficulty.

Salvarsan Milk.—Jesionek (*Münch. med. Woch.*, 1911, lviii, 1169) has observed cases similar to those of Taege, Duhot, and others, in which the suckling infant of a syphilitic mother was apparently cured of lues following the administration of salvarsan to the mother. Unlike previous observers, however, Jesionek has demonstrated arsenic in the milk of the syphilitic mother after treatment with salvarsan. He believes the benefit to the infant may be due quite as much to the arsenic as to the antibodies in the milk. Furthermore, there is the possibility that the milk may contain endotoxins. To eliminate antibodies and endotoxins, the author injected salvarsan intravenously into a goat and used the milk, which, however, did not yield an arsenic mirror, as food for a child of five years suffering with acquired lues. There were marked lesions of the skin and mucosæ, including condylomata. The child received no other treatment. There was a rapid and complete symptomatic cure coincident with the taking of the milk.

A Blood Counter for Leukocytes and Cytodiagnosis.—R. Dunger (*Münch. med. Woch.*, 1911, lviii, 1131) has enlarged the ruled area of the hemocytometer so that it covers forty-nine instead of nine square millimeters. He used the Türck ruling. The chief advantage of the counter is in cases with marked leukopenia and in the cytodiagnosis of serous fluids, especially cerebrospinal fluids, in which the cells are few in number. The apparatus is made by Zeiss.

On New Characteristics of the Urine in Health and Disease.—H. Pribram (*Deutsch. Arch. f. klin. Med.*, Leipzig, 1911, cii, 457) has made interesting observations, injecting various portions of normal and

pathological urines into rabbits and noting the effects. He finds (1) that the injection of urine gives rise to the formation of hemolysins, precipitins, and complement binding antibodies in the serum of the injected animal. The precipitin formation is always more marked with the injection of normal urines than with albuminous; the fixation of complement, on the other hand, is greater when one uses albuminous urines for injecting the experimental animals. (2) The injection of urinary sediment and of the alcohol-ether insoluble portion of the non-dialyzable fraction ("lysogenous substance") of the urine produce the same changes in the serum of the injected animal as described under (1). (3) The "lysogenous substance" contains the normal urinary albumin and a number of other substances. In chronic nephritis this fraction is practically normal, whereas in acute nephritis its increase runs parallel to the amount of albumin. (4) Both qualitative and quantitative examination of this fraction show that its chief constituents are not albuminous. (5) The substances in the urine which act as antigen probably arise in the renal cells. (6) The urine is markedly toxic. The same is true of the lysogenous substance and of the sediment. Repeated injections seem to raise the resistance of the animal to the poisoning. (7) The symptoms of uremia are possibly due to a retention of the toxic bodies contained in the lysogenous substance. (8) The "Mörner fraction" of the urine contains traces of lysogenous bodies, but no precipitin or complement binding antigens, and is not toxic to animals. In the examination of the urine of 50 patients with hypertension, the usual heat and acetic acid test showed a trace of albumin in 15, the acetic acid and heat in 36 cases. In other conditions with a trace of albumin similar results were secured with the two methods of employing acetic acid.

The Acetonitryle Reaction in Basedow's Disease.—G. Ghedini (*Wien. klin. Woch.*, 1911, xxiv, 736) has made an experimental and clinical study of the acetonitryle reaction of Reid Hunt. The latter found that the feeding of thyroid to white mice greatly increased their resistance to the poisonous effects of acetonitryle. Ghedini has used the blood of patients with a variety of diseases as food for mice. It is of interest that in three well-marked cases of Basedow's disease the reaction was strongly positive, whereas in two doubtful cases (formes frustes) the resistance of the mice remained unchanged.

The Wassermann Reaction in Lead Poisoning.—A. Dreyer (*Deut. med. Woch.*, 1911, xxxvii, 786) has examined sera from a number of cases of lead poisoning. Of 35 cases of plumbism, 4 gave a positive Wassermann reaction; 25 were tested according to Stern's modification of the Wassermann technique, and of these, 12 were positive. The positive cases gave no history of syphilitic infection nor could signs of lues be found on physical examination. The author believes the positive reactions were due to the lead poisoning *per se* and not to a latent lues.

A Urinary Reaction in Progressive Paralysis.—H. M. Stucken (*Münch. med. Woch.*, 1911, lviii, 855) has repeated the work of Butenko, who found that the urine of patients suffering with progressive paralysis gave a characteristic reaction with liquor Belostii. Stucken finds the

reaction positive in a great many diseases other than progressive paralysis and in the latter his positive findings were proportionally much lower than Butenko's. He, therefore, concludes that the reaction is without diagnostic value.

On the Transmission of Scarlatina to the Chimpanzee.—Landsteiner, Levaditi, and Prasek (*Compt. rend. Soc. de biol.*, Paris, 1911, 641) have made several attempts to infect a chimpanzee with virulent matter from a child suffering from scarlatina. In their first experiment the throat of the chimpanzee was painted with material taken from the tonsils and pharynx of children suffering with scarlet fever with angina. This was followed in two days by a redness and swelling of the tonsils, fever, and presence of streptococci in the tonsillar secretions. Four days after the inoculation the throat was painted again and 75 c.c. of defibrinated blood taken from a severe case of scarlet fever were inoculated. Two days later there were redness and intense swelling of the pharynx, tonsils, and pillares of the fauces; white deposits on the tonsillar mucosa, and a general exanthem. The animal was very ill and died three days later. Abscesses formed at the point of inoculation of the blood. Autopsy: Swelling of the cervical glands and mediastinal glands; points of interstitial inflammation in the kidneys; lesions of the skin resembling those in scarlet fever. In the second case the injection of 50 c.c. of scarlatinal blood under the skin and painting of the throat as before was followed in forty-eight hours by slight fever and tonsillitis. There were no general phenomena. Reinjection ten days later produced tonsillitis again. Inoculation of streptococci isolated from the throat of these chimpanzees produced no result in the throats of others. In other words, painting the throats of the chimpanzee with products coming from scarlatinal children provokes an angina similar to that of patients suffering from scarlet fever, but it is not certain whether this angina is produced by the scarlatinal virus or by some other infection. While the observation is single and insufficient in itself, the authors point to the advisability of further experiments of the same nature.

Use of Urotropin in Pneumonia.—Shattuck (*Bost. Med. and Surg. Jour.*, 1911, clxiv, 842) reports his experience with the routine use of urotropin in pneumonia. It was originally given as a preventative for empyema in doses of 10 grains, *t. i. d.*, but after a study of 59 cases treated with the drug, as compared to 188 not treated with it, the incidence of empyema was certainly not lowered. The hopeful feature of the treatment is the fact that no pericarditis or otitis media developed in any of the cases.

Antityphoid Vaccination per Rectum.—Courmont and Rochaix (*Presse Méd.*, 1911, 453) have vaccinated men per rectum against typhoid fever instead of subcutaneously. A bouillon culture of Bacillus typhosus was killed by heating to 53° C. After a preliminary evacuant enema, the patient was given 100 c.c. of this suspension of dead bacilli through a high rectal tube, 15 drops of laudanum being added to facilitate retention. The enema was retained about twenty-four hours. In no case was there fever, malaise, colic, or backache. The enemata

were repeated at the end of five and ten days. After a period of ten days the serum of the individual showed marked changes to the Bacillus typhosus. The agglutinative power had risen to 1 in 30; the bacteriolytic to 1 in 20, while the bacteriocidal power soon reached 1 in 1000. Should this method, after due trial, prove effectual, objection to antityphoid vaccination would be reduced to a minimum, for all complaint has been based upon pain in the joints and backaches, the malaise and fever incident to the first subcutaneous inoculation.

Treatment of Diabetics with Soda Bicarbonate, Intravenously.—Lépine and Labbe have for some time advised the treatment of diabetics in coma or showing premonitory signs with soda bicarbonate, intravenously. Sicard and Salin (*Bull. et Mém. Soc. Méd. d. hôp. de Paris*, 1911, xxviii, 854) now advocate its use in certain diabetic conditions dissociated from coma, such as pruritus and muscle pains, but which have resisted dietetic and medicinal efforts. They have used much stronger solutions with great success, and observe that a solution of 9 or 10 per cent. in place of 1 or 3 per cent. is well borne by the patient and can be freely repeated. The solution is, of course, sterilized in a closed flask and used in amounts of 100 to 250 c.c. This represents in 100 c.c. about 10 grams, or 280 grains, of the bicarbonate. The injection is made into the veins of the arm, but the greatest care must be exercised not to get the solution into the surrounding tissues, because it is very caustic. The possibilities of such concentrated doses are much increased when one remembers that in coma or in cases showing premonitory signs, it may be necessary to use large doses of bicarbonate, and at the same time avoid raising blood pressure by injections of great volume.

Angina Pectoris with Vasomotor Excitability.—MacKenzie (*Heart*, 1911, ii, 265) has observed a man, aged thirty-five years, who had rheumatic fever and syphilis. For five years he had frequent attacks of pains in the chest, with fever, nausea, and palpitation, coming on even when he was quiet. He always avoided motion and generally had a pulse of 70 to 90 per minute, and blood pressure of 130. The heart was enlarged and gave clinical evidence of aortic regurgitation and stenosis. The pain was typical in distribution to the left chest and arm. In an attack the pulse rate rose to 120 and the pressure to 240, varying directly with the severity of the pain. Following the administration of amyl nitrate, the pressure sank to 150, coincident with the cessation of pain, but pressure rose and pain returned as the effects of the drug wore off. Morphine and chloroform produced similar effects. Realizing that the nervous system was at fault, as shown by the vasoconstrictor mechanism, he was given bromides with good effect. At autopsy aortic regurgitation and hypertrophy were found, with no great involvement of the coronary arteries. The association of aortic valve disease with angina is well known, and this case presents the typical features of arterial constriction, more marked in cases of aortic valvular disease than in other forms of angina. In all forms of angina much more efficient results can be obtained by attention to the nervous system than by cardiac therapy, and bromides are ideal for such a purpose.

SURGERY

UNDER THE CHARGE OF

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Disinfection of the Field of Operation in Abdominal Operations.—Propping (*Zentralbl. f. Chir.*, 1911, xxxviii, 661) says that the increased occurrence of mechanical obstruction since the introduction of iodine disinfection led him to question whether this use of iodine could play a causal role in the production of the obstructions. Iodine is an excellent substance with which to produce adhesions between serous surfaces. Propping established the following facts: If, a half-hour after coating the skin with iodine, a cloth moist with saline solution is laid on the browned skin for half a minute, the cloth at the area of contact will give with starch a strong iodine reaction (blue discoloration). Even when the cloth touches the browned skin for only a moment, the iodine reaction can be produced, although weaker. If in an animal experiment the intestines are laid a short time on the iodine stained skin, the intestines will give the iodine reaction. One can obtain the same result in man with the extirpated appendix. The field of operation toward the end of the operation, especially when it has been handled with fluids, as saline solution, is almost always deprived of its color. This faded area will no longer give the iodine reaction. Therefore the iodine must have passed to the surrounding regions and structures. In animal experiments (on rabbits), according to R. Heinz, very small amounts of iodine injected intraperitoneally will produce in a short time abundant layers of fibrin and firm membranes and bands between the intestines. The effect is to a certain degree specific, in contrast to that of turpentine. Propping injected intraperitoneally in a dog 20 drops of the tincture of iodine, dissolved in 80 c.c. of sterile saline solution, and found after forty-eight hours, in the region of the liver and stomach, abundant fibrous adhesions. There were no adhesions in the region of the small intestines. Evidently dogs are little suited to the development of experimental adhesions, on account of the activity of their intestinal and body movements. The abdominal cavity in the human subject, on the other hand, inclines especially to adhesions, particularly from a moderately specific irritation, as from gonorrheal infection. Propping has, since the introduction of iodine disinfection, in about 70 cases of appendicitis, simple or complicated with abscess or peritonitis, 6 times found ileus from kinking or adhesions. This was unusual before the use of iodine for this purpose. Of about 300 cases of appendicitis in 1910 and 1911, before the introduction of iodine

disinfection, there were only 5 cases of mechanical intestinal obstruction. He concluded that eventration of the intestines directly upon the browned skin should be absolutely avoided. They should be laid on interposed layers of gauze moist with saline solution. Whether this will be sufficient to prevent harmful effects from the iodine must be determined by further observations.

Cystoscopic Diagnosis of Syphilis of the Bladder.—Haberern (*Zentralbl. f. Chir.*, 1911, xxxviii, 663) refers to the quotation from Nietze in the scanty literature on this subject, to the effect that a syphilitic process in the bladder has not yet been established by the cystoscope. Nietze, however, believed that the future would show that, notwithstanding the older literature, the bladder was not completely immune to the virus of lues. Haberern reports the case of a woman, aged forty-one years, who had had, for fourteen years, an ulcer on the tongue, which healed very slowly under the application of caustics. At the same time she had pain in the throat and dysphagia, which lasted a long time, and since then she has been speaking with a nasal twang. Later she had similar chronic ulcers on the thigh. For four years she has been having frequent micturition, urinating during the day every three-quarters to an hour, during the night every two hours. The condition has been growing worse during the last few months. The urine is bloody at the end of micturition, which is followed by pain. Examination at the hospital showed absence of the uvula and left half of the palatoglossal arch, and several contracted scars in the throat. If the patient was placed in a somewhat bent forward position, fluid taken into the mouth passed out again from the nose. The Wassermann reaction was positive. The cystoscopic examination showed the bladder wall smooth and glistening. The openings of the ureters were normal. The wall of the sphincter was swollen and uneven, and close behind it there was a round ulcer the size of a walnut. On its left side there was a tumor, three or four points on which were tubercular and all but one covered by mucus membrane. At the most prominent part of its surface it was ulcerated and suppurating. This was diagnosticated as a gumma. An injection of Ehrlich's arsenobenzol was given. Twenty days after the injection a cystoscopic examination showed that the bladder wall was not smooth and shining as before the injection, but was hemorrhagic in places. Fine trabeculæ were visible on the lateral wall and vertex. The tumor at the sphincter was entirely smooth. Five weeks after the injection the patient was discharged from the hospital in good general condition and free of urinary disturbances. Before her discharge the cystoscope showed the swelling at the sphincter and the gumma reduced to a small smooth protuberance. The urine was almost normal.

The Displacement Posteriorly of the Prominent Premaxillary Bone in Complicated Harelip without Drawing in the Tip of the Nose.—Reich (*Zentralbl. f. Chir.*, 1911, xxxviii, 859) says that when the premaxillary bone is especially prominent in a double harelip, its displacement backward is accompanied by a pulling on the nasal septum and with it the tip of the nose, a pug nose being thus produced. To overcome this tendency Reich operated on a child, aged three months,

in the following manner: The profile of the nose was normal, but after dividing the vomer and pushing back the premaxillary bone into the gap in the alveolar arch, a marked deformity was produced from the pull on the tip of the nose. The stunted median portion of the lip was then separated from the premaxillary bone. An incision was made directly upward as far as possible through the mucous membrane, perichondrium, cartilaginous septum, and perpendicular plate of the ethmoid bone. The bleeding was slight. There remained along the bridge of the nose a broad piece of bone and cartilage, which maintained the existing profile of the nose, because it did not accompany the backward displacement of the premaxillary bone. In order that the mucoperiosteum of the nasal wall may not resist this backward movement it is first divided. The vomer behind the premaxillary bone is then divided subperiosteally and in a V-shape before pushing the premaxillary bone back to its proper place. The nourishment of the remaining portion of the vomer is aided by making this V-shaped excision subperiosteally, the nasopalatine artery being thus preserved. After the premaxillary bone is placed in its proper place it is fixed in position by the repair of the harelip. This should provide two short lateral incisions in the cheek, according to the method of Mirault for mobilizing the lateral flaps. The median piece of the lip which has been separated upward is employed to complete the normal septum. The result of the operation was good. There was absent the flattening due to extirpation of the premaxillary bone, which now filled the defect in the alveolar arch. The disturbance in the development in the upper jaw when the premaxillary bone is removed was not seen. The nasal septum was high, the tip of the nose not drawn in, and the profile of the nose was good.

Myonephropexy.—Jiano (*Ann. d. mal. d. org. gén.-urin.*, 1911, i, 981) did the following operation for a movable kidney on the right side in a woman, aged fifty years. The patient was placed in the left lateral decubitus, with a cushion under the flank to render the right side prominent. The left lower extremity was flexed upon the abdomen and the right placed in extension. Spinal anesthesia was employed. An incision was made along the external border of the erector spinæ muscle, beginning at the lower border of the tenth rib and ending 2 cm. above the iliac crest. The incised skin was dissected on both sides from the underlying muscles for about 5 cm. An incision was then made through the first plane of muscles formed by the latissimus dorsi and the small inferior serratus. On the internal side of the wound these muscles were dissected up from the erector spinæ. From the latter were cut two muscle strips, one short and one long, and both one to two centimeters wide. Then the other muscle layers were divided and the kidney exposed. The latter was brought to the surface and decapsulated over an area of 2 cm. The isolated muscle strips were passed transversely under the kidney, as a support for the latter. The distance between the two muscle strips was from 3 to 4 cm., which allowed for the hilum of the kidney. A catgut suture was passed through the free end of each muscle strip. In the upper part of the wound, about 5 cm. from the external edge, the muscle flap is penetrated by a Reverdin needle from without inward. The needle is then threaded

with one end of the catgut suture of the first muscle strip and the suture drawn through the muscle flap. The other end is drawn through in a similar manner, a half centimeter away. Both ends being tied together, the first muscle strip is fixed, thus supporting the superior pole of the kidney. Three or four centimeters lower, the other muscle strip is fixed in a similar manner. A transverse bridge is thus formed for the support of the whole kidney. To prevent movement of the kidney, the edges of the stripped-up capsule are fixed on each side to the muscle strips. The abdominal wall is then closed with sutures. Eleven days after the operation the patient left the hospital completely cured. Jiano concludes that myonephropexy is an operation easy of performance and absolutely benign. It assures a good fixation of the kidney without any disturbance in the escape of urine. It dispenses with all inconvenient products owing to the permanence of the supports—pain, suppuration, fistulæ, and the formation of sclerotic tissue in the renal parenchyma.

Concerning a Case of Invagination of the Ileum Cured by Resection: A Contribution to the Treatment of Intussusception.—Haagn (*Deut. Zschr. f. Chir.*, 1911, 142) says that the general tendency is to regard total resection as indicated only when all other methods of treatment have failed. He reports a case in which, after exposure of the intussusception which involved the ileum about a hand's breadth from the cecum, it was found impossible to reduce the invagination. It was resected and the bowel ends united by circular suture. The patient recovered and was discharged one month after the operation. Three months later the patient was again examined and found well, and six months pregnant. She was delivered successfully. Leichenstern found that in 479 cases of invagination spontaneous reduction of the invagination occurred in 15 cases; also in 15.6 per cent. of the cases of invagination of the ileum, with a mortality of 42.6 per cent. We cannot, therefore, rely upon this method of treatment. Haagn agrees with Rydigier in the following conclusions on the treatment of intussusception: In acute invagination operation should be performed as soon as possible after properly employed non-operative measures have been tried without success. When a laparotomy has been done, disinvagination is to be preferred when it can be carried out without special difficulty. If the intestinal wall at any place in the area of invagination is suspicious, a strip of iodoform gauze should be introduced to this place or the affected area excluded from the abdominal cavity. Resection of the whole invagination is indicated when the intestinal wall shows marked changes or threatens perforation. The employment of an artificial anus, or entero-anastomosis, is to be condemned. Haagn believes that in ileocecal and colon invagination, when disinvagination has been difficult and the serous surface of the intussuscipiens is intact, the intussusceptum may be resected. In case, however, the invagination is only a short one, a total resection should be done, because of the better prospects of a radical cure, although one should also take into account the general condition and age of the patient. If very short, unless reduced with very little difficulty, resection is to be preferred to all other methods. But even when the invagination is easily reduced, a secondary resection must be kept in mind, since it is the only sure means for the prevention of a recurrence.

THERAPEUTICS

UNDER THE CHARGE OF

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Irritation of the Kidneys by Salicylates and its Prevention by the Administration of Alkalies.—Glaesgen (*Münch. med. Woch.*, 1911, lviii, 1125) has found that the salicylates induce an albuminuria when given alone. The administration of from 6 to 10 grams of sodium bicarbonate in the course of twenty-four hours is sufficient to prevent this albuminuria. Thus the kidneys are saved, which may be of distinct advantage in the treatment of patients who have had a previous kidney lesion. The therapeutic action of the salicylate did not seem to be modified by the alkali. In general, twice as much of the alkali as of the salicylate was necessary to prevent this albuminuria in the cases studied by Glaesgen.

The Treatment of Anemia with Salvarsan.—Leede (*Münch. med. Woch.*, 1911, lviii, 1184) reports a case of severe anemia that closely simulated pernicious anemia in which great improvement was obtained by injections of salvarsan. Subsequently the Wassermann reaction indicated that the anemia was of luetic origin. Leede has also treated undoubted cases of pernicious anemia with absolutely no benefit. The results were fatal in 5 cases treated, although in 4 the treatment was given as the last resort. Leede thinks that if salvarsan benefits markedly any case of severe anemia, it is of diagnostic value and points to a luetic basis for the anemia.

Fatalities after Injection of Salvarsan in Patients with Cardiovascular Disease.—Martius (*Münch. med. Woch.*, 1911, lviii, 1067) has collected 18 cases where death followed the injection of salvarsan in patients suffering from some form of cardiovascular disease. He reports the details of these fatalities, and in analyzing, them in order to ascertain the cause of death, he concludes that in only 7 cases death occurred as a result of the injection. In 5 of these 7 cases the autopsy findings showed the triad, syphilitic aoritits, sclerosis of the coronary arteries, and myocardial degeneration. In 1 case there was found myoplasia of the heart and aorta. The seventh case showed severe pathological changes in many of the organs. Four of these fatal cases showed no objective signs during life of any cardiovascular trouble. Martius concludes that syphilitic aortitis, especially if complicated with coronary arteriosclerosis or myocarditis, is an absolute contraindication to the use of salvarsan. He thinks that angina pectoris, unless associated with changes in the heart muscles, is not a contraindication, and even may be favorably influenced by the injection of salvarsan. Martius says that there is absolutely no danger in giving salvarsan by intravenous injection to patients with sound hearts and arteries, provided that the remedy is given well diluted.

The Treatment of Pernicious Anemia.—Effendi (*Deutsch. med. Woch.*, 1911, xxxvii, 930) relates the history of a patient suffering apparently from pernicious anemia. When first observed the red blood cells were 1,280,000; the white cells, 4800; and the hemoglobin 38 per cent. Because of the history of a previous luetic infection, active antiluetic treatment was given, but the anemia progressed. Iron and arsenic also had no effect, and the red blood cells fell to 970,000, with 20 per cent. of hemoglobin. Effendi then tried glycerin in doses of a tablespoonful three times a day, and later this dose was increased to 70 grams. The improvement was rapid, and at the end of a month the red blood cells were 4,200,000, with 100 per cent. of hemoglobin. Since then the patient has remained perfectly well, and the red blood cells have increased still further, to 5,200,000. Effendi was led to try this method of treatment by the report of a case of pernicious anemia similarly treated by Tallquist, who had equally good results. He does not think that glycerin will cure every case of pernicious anemia, but believes that it may benefit only those of intestinal origin.

Salvarsan in the Treatment of Malignant Tumors.—Von Czerny and Caan (*Münch. med. Woch.*, 1911, lviii, 881) have tried salvarsan in the treatment of various malignant tumors. They found that salvarsan had a distinct beneficial effect upon inoperable malignant tumors, especially upon sarcoma when the Wassermann reaction was positive. They observed a considerable diminution in the size of sarcomatous tumors, together with an improvement in the general condition. The cases of carcinoma showed no objective signs of improvement, although marked diminution of pain and a considerable general improvement usually followed the injections. They suggest that salvarsan therapy may be of value after the surgical removal of sarcoma in order to prevent a probable recurrence. This treatment is contraindicated in cachectic and in very weak patients. They believe that it may be possible to increase the dose of salvarsan for the treatment of malignant tumors, and then better results may be obtained. Usually a single dose of from 0.4 to 0.6 gram salvarsan was given, and they question whether a number of small repeated doses of salvarsan would not have had greater therapeutic effects. The question is also raised as to the effect of local injections of salvarsan into the tumor combined with the remedy given in the usual manner.

The Therapeutic Use of Pituitrin.—Klotz (*Münch. med. Woch.*, 1911, lviii, 1119) reviews the work of many different observers regarding the action of pituitrin in raising abnormally low blood pressure. From his own clinical observations and experimental work on animals, Klotz is very favorably impressed by the beneficial effects of pituitrin in conditions that are associated with lowered blood pressure. He recommends it especially in uterine hemorrhage due to postpartum atony of the uterus. He also thinks it may be of value in other hemorrhages dependent upon a low vasomotor tone and in postoperative shock, although he has no personal experience with its use in such conditions. Klotz also suggests that it should be used in conditions of low vasomotor tone due to the toxins of acute infectious diseases. He says that pituitrin has the marked advantage over adrenalin, in

that its action is more moderate but prolonged over a greater period of time. There are no untoward by-effects from its use, but he advises against giving it to patients with abnormally high blood pressure. Pituitrin may be given by mouth in doses of 0.2 gram of the fresh gland substance, or it may be obtained in a form suitable for intramuscular injection. The latter method seems to have a more certain and more rapid action.

Some Observations Concerning Veronal.—Von Noorden (*Therapie d. Gegenwart*, 1911, lii, 287) says that veronal is more certain in its action than most of the other hypnotics. He also believes that it is perfectly safe when given in proper dosage. A certain degree of depression, dizziness, and headache have seemed to follow the use of veronal, but von Noorden thinks that these after-effects may be ascribed to the fact that larger doses than necessary were employed. He advocates combining small doses of phenacetin with veronal. He believes that when given in such a combination, a much smaller dose is necessary for hypnotic effect and the unpleasant after-effects are avoided. Von Noorden says that 0.3 gram of veronal combined with 0.25 gram of phenacetin has the same hypnotic action as 0.6 gram of veronal when given alone. When insomnia is accompanied by cough or pain, the addition of small amounts of codeine also enhances the hypnotic action of veronal.

The Towns-Lambert Treatment for Morphinism and Alcoholism.—Cabot (*Bost. Med. and Surg. Jour.*, 1911, clxiv, 76) speaks highly of the Towns-Lambert method of treating morphinism and alcoholism. He has already seen results sufficient to confirm him in the belief that, aside from suggestion and any notable psychical impressions, the treatment has great value, especially for patients with the morphine habit.

Iodides in High Blood Pressure and Arteriosclerosis.—Matthew (*Edinburgh Med. Jour.*, 1911, vi, 228) believes that iodides have a noticeable effect in lowering blood pressure in patients with high blood pressure but without arteriosclerosis. He says that they are useless in increased blood pressure associated with advanced arteriosclerosis. The initial dose of potassium iodide must be 0.6 gram in order to obtain any lowering of the blood pressure, and this dose must be rapidly increased in order to secure its maximum action. Matthew thinks that the organic preparations of iodine in the ordinary therapeutic doses as given contain too little iodine to be of any value as vasodilators. They should only be given when the iodides are not well borne by the gastro-intestinal tract. The best of the organic preparations seems to be sajodin.

Lipanin as a Substitute for Cod-liver Oil in Rachitis.—Schabad and Gurochowitsch (*Monats. f. Kinderheilkunde*, 1911, ix, 659) say that the action of cod-liver oil in rachitis has been theoretically explained by its rich content of free fatty acids. Acting upon this assumption, Mering has introduced to us a substitute for cod-liver oil—olive oil with the addition of 6 per cent. of free oleic acid. This may be obtained

under the trade name lipanin. The authors have investigated the therapeutic action of lipanin in rachitis especially with reference to any possible action upon the metabolism of the mineral salts, and have come to the following conclusions: (1) Lipanin as well as olive oil increases the absorption of nitrogen and of fat, but lipanin is not superior to olive oil in these respects. (2) Lipanin has no influence whatever upon the calcium metabolism in rachitis, and therefore cannot replace cod-liver oil in the treatment of rachitis.

The Physician's Attitude toward New Remedies.—Heubner (*Therap. Monatshefte,* 1911, xxv, 402) sounds a warning regarding the overproduction of new proprietary remedies often differing but slightly in chemical structure and to which are attached names that are so entirely different that their close relationship is concealed. He gives the formulas of six very closely allied remedies as regards their chemical structure, as an example of this practice. These remedies are anesthesin, profesin, cycloform, neuronal, adalin, and bromural. Heubner says that this practice has the bad effect of burdening the memories of practising physicians with a long list of names of remedies that differ but slightly, if at all, in their physiological action. He cites other examples of this practice, such as applying the name medinal to veronal natrium. Heubner says that most of these drugs have some therapeutic action, but are not superior to the old tried remedies. Furthermore, all these new remedies lack sufficient critical trial to justify their supplanting the old remedies, and their increasing number necessarily prohibits the thorough trial of a remedy before a new modification is brought forward.

The Results of the Treatment of Tetanus with Subcutaneous Injections of Carbolic Acid.—Bacelli (*Berlin. klin. Woch.,* 1911, xlviii, 1021) reviews the results obtained by a large number of different clinicians who used subcutaneous injections of carbolic acid for the treatment of tetanus. Bacelli was the first to advocate these injections for therapeutic purposes, and he makes use of a 2 or 3 per cent. solution of carbolic acid injected either subcutaneously or intravenously. He says that it is possible to give from 0.5 gram to 1 or 1.5 gram of carbolic acid to patients suffering from tetanus. These doses are divided in the course of twenty-four hours, and the urine is closely watched for possible toxic effects. Bacelli says that patients with tetanus tolerate these large doses of carbolic acid remarkably well. He gives the details of 94 cases of severe tetanus and 38 cases of very severe type treated by this method. Of the 94 severe cases only 2 per cent. died, and the mortality in the very severe cases ranged from 19 to 15 per cent. The entire number of patients treated by this method, as reported in the literature, is 190. There were 33 fatal cases in the whole series, thus giving a mortality percentage of 17.36. Bacelli says that the dose of carbolic acid given to many of those patients who succumbed was entirely too small. One of the fatal cases was due to a gangrene of the arm, following the injection of the carbolic acid. Bacelli believes that the results obtained by this method of treatment are far superior to those obtained by the therapeutic use of tetanus antitoxin.

PEDIATRICS

UNDER THE CHARGE OF

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The Serodiagnosis of Anterior Poliomyelitis. — EDWARD MILLER (*Deut. med. Woch.*, 1911, xxxvii, 1105) points out that the clinical interest in the experimental immunization of apes to anterior poliomyelitis by a serum lies in the fact that this indicates the presence of antibodies in human beings who have recovered from anterior poliomyelitis, and that it makes possible a serodiagnosis of epidemic anterior poliomyelitis. The latter would be of great value, especially in the abortive form of the disease. Müller and Römer have made investigations which have convinced them that these antibodies develop also in human beings in conjunction with epidemic anterior poliomyelitis and remain in the blood for many years. Active virus from apes was mixed with the serum of an immunized human being for many hours and then injected intracerebrally in apes. Controls received in the same way virus mixed with serum from individuals who never had anterior poliomyelitis. The controls contracted the disease, while the test cases escaped, presumably because of the antibodies present in the immunizing serum. Miller examined a typical case of abortive anterior poliomyelitis. The clinical diagnosis of this form rests on the fact that in an epidemic several children in one family show identical prodromal symptoms; but one of them fails to develop the paralysis which attacks the others. Using the serum from this case in the test stated above, he found the serodiagnosis positive, thereby substantiating the clinical diagnosis and proving that this form of anterior poliomyelitis does exist. This coincides with the results obtained by Anderson Frost, who found in an epidemic 9 cases which had suspicious prodromal symptoms; but which developed no paralysis. They neutralized an emulsion of active virus six times with the blood serum of these cases. It is still a question whether the predisposition to the disease found in children is that of the spinal cord or the portal of entry. The liability of the lymphatic system to disease in children, and the hypothesis that the virus is carried to the spinal cord through the lymphatics favor the former idea, while the latter possibility has been rather neglected. Just as a positive reaction in this serodiagnosis indicates an abortive case of anterior poliomyelitis, so does a negative reaction absolutely indicate the absence of poliomyelitis infection. This fact Müller demonstrated in another series of experiments. In proof that there is no etiological difference in the sporadic and epidemic forms of the disease, Müller reports that the serum from a case which had the sporadic form six years before neutralized the virus of the epidemic form exactly the same as did the serum of the epidemic form. This serodiagnosis may well prove to be highly important in tracing the origin of widely separated local epidemics. Owing to the expense, the difficult technique, the length of time necessary, and the possibility of errors due to using unrecognized abortive

cases for controls, this method of serodiagnosis is rather applicable to the development of research work than to general practice and isolated cases. The clinical value of the method, however, is greater in children than in adults. The method would seem most valuable in recognizing sporadic cases disguised as Landry's paralysis or acute bulbar paralysis of childhood. The antibodies which have been demonstrated as early as the sixth week after infection, exist and may be found for years afterward, and this method of serodiagnosis will become of paramount importance to the pathological and histological methods of diagnosis. The therapeutic value of an antiserum in this disease has so far proved negative.

The Treatment of Early Infantile Paralysis by Immobilization.—E. Mayer (*Deut. med. Woch.*, 1911, xxxvii, 1107) adds an important feature to the local treatment of the paralyzed parts in anterior poliomyelitis by describing MacKenzie's method of immobilization. Up to the present time the usual treatment of this disease has been rest in bed, hydrotherapy to combat fever, and pain and, locally, inunctions of mercury. Krause, believing the gastro-intestinal tract to be the avenue of infection, recommends calomel to disinfect the intestines. After the acute stage has passed, the paralyzed parts are usually massaged, treated by electricity, and eventually placed in splints. While some cases are cured by this treatment, yet the greater percentage are uninfluenced by it, and subsequently exhibit the most pitiful contractures and paralyses. The contractures arise from the recovery of one set of muscles without the recovery of the opposing muscle group; from long continued crooked positions of the patient in bed, or from the pressure of the bed clothing. The development of a pes equinus, for instance, can often be avoided if the foot is protected from the weight of the bedclothing. In the light of the relatively poor results from the routine treatment, the proposition of MacKenzie is highly interesting. He recommends, where paralysis occurs in the upper extremity, that the muscles, immediately on being affected, be placed at rest by splints and kept so for weeks or months. Also that the position be such as to relieve the muscle of any functional movement. By absolute rest in bed, the position and angle of the splint is gradually changed. In 10 patients coming under observation during the first ten days, MacKenzie reports 9 as being cured by this method. In 3 of the cases a good result was apparent in from four to seven weeks up to eight months of treatment, with rest in bed and splints. Five cases treated with massage and electricity for over three months showed no sign of improvement. MacKenzie believes that with his method a subsequent mechanical or surgical treatment is unnecessary. Mayer, in introducing this method, suggested its use also in the lower extremity, and the use of a plaster-of-Paris mould instead of splints. The use of plaster mould tends to prevent severe degrees of contracture and the formation of exudates. Mayer reports 2 cases in which he used the new method. One case had paralysis of the arms, legs, and back. Improvement was pronounced in four weeks. In two months the child had entirely recovered except for a slight paralysis of the tibialis anticus. Another case with one leg affected and with paralysis of the quadriceps recovered in four weeks. This method of immobilization with plaster tends to avoid reflex irritation of the spinal cord.

OBSTETRICS

UNDER THE CHARGE OF

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The Unfavorable Influence of Pregnancy upon Chronic Progressive Deafness.—Brickner (*Amer. Jour. Obstet.*, June, 1911) finds that, although the pathological process present cannot be clearly made out, pregnancy in women suffering from chronic progressive deafness becomes a serious matter and increases the deafness. This bad effect is evident so soon as pregnancy begins, increases during gestation, and remains permanent after delivery. Repeated pregnancies make the hearing progressively worse. If pregnancy be interrupted the hearing may temporarily be better, but subsequently will deteriorate. Abortion should be induced as soon as it is evident that pregnancy is injuring the hearing. It might be justifiable, at the request of the patient, to render impregnation impossible.

The Influence of the Automobile upon Obstetrical Conditions.—Edgar (*Amer. Jour. Obstet.*, June, 1911) has investigated the subject of the use of the motor car upon obstetric conditions. He believes it to be true that the motor car causes more vibration than any other vehicle; the distance traversed at one sitting is almost invaribaly greater with the motor car than with the horse-drawn vehicle, and the patient is almost unconsciously exposed to considerable strain. The effect of the motor car on the nervous and circulatory systems is very different from that produced by other vehicles. Some patients seem but little disturbed even though high speed is used and long runs are made, and minor accidents on the road may occur. Such patients can usually be allowed to use a motor car during pregnancy, if very careful to avoid actual physical fatigue, and do not use the motor at the times corresponding to the menstrual periods. Other patients are made intensely nervous and excited by the use of a motor car, with rapid pulse and often insomnia. The continuous use of the motor car tends to produce constipation, and hemorrhoids are made worse by motoring. Pelvic or abdominal congestion or inflammation is made worse. Pyelitis and appendicitis are aggravated. Displacements of the uterus and subinvolution are also made worse. If the motor car be used immediately after abortion or labor, subinvolution may be caused and backward displacements aggravated. In many anemic women, who are too flabby to take exercise, the motor car has proved a positive benefit, and in cases where prompt treatment is necessary the motor car has undoubtedly assisted in the saving of life.

The Susceptibility of Pregnant Women to Tuberculin.—Bar and Devraigne (*L'Obstétrique*, April, 1911) believe, from their investigations, that pregnant women have diminished sensibility to the reaction of

tuberculin. This diminution does not seem to exist during the entire period of pregnancy, but seems most pronounced during the last months of gestation.

Sacro-iliac Relaxation.—Meisenbach (*Surg., Gyn., and Obstet.*, May, 1911) has made the study, from the standpoint of orthopedic surgery, of this condition, and publishes a well-illustrated paper, with analysis of 84 cases. He concludes that the sacro-iliac joint is a true joint, normally admitting some motion. It may be subjected to strain or complete sublaxation as well as to the diseases which affect other joints. The pelvic girdle is the main support of the trunk, and when relaxed may jeopardize the sacro-iliac joint, loosening the sacrum or causing an actual dislocation. Sciatica often results from the slipping of the sacro-iliac joint, and many of the backaches from which women complain are caused by sacro-iliac strain. An habitually abnormal attitude and also flat foot in young and old, may predispose to strain of the sacro-iliac joint. The degree of motion in this joint varies greatly, and is usually more marked in walking. Strain upon these joints may be produced by a pendulous abdomen and direct or indirect muscular violence or general debility may further partial dislocation of the joint. A diagnosis should be made of this condition as early as possible, as its prompt relief may prevent distressing and prolonged nervous disturbances. In acute cases, with sharp pain and spinal curvature, early treatment may give immediate relief. All cases must not be subjected to fixation, as the success of treatment will depend upon the detection of the cause. In these cases the pelvic girdle must be supported, and thus strain upon the joints be relieved. This subject is of practical interest to the obstetrician, because relaxation in the sacro-iliac joints following labor is not uncommon. The more severe the labor, the more poorly developed and anemic the patient, the greater is the liability to this complication. Inability to walk, fatigue, indefinite pain, especially upon turning in bed or rising from a chair, are the principal symptoms. The patient will usually refer this pain to the affected region, and if she be lying upon a firm bed or table, pressure over this joint will cause pain. Sacro-iliac relaxation is a complication of considerable importance after difficult forceps deliveries and especially after symphysiotomy or pubiotomy. Cases in which the occiput rotates posteriorly in labor are more apt to be followed by this condition than is normal labor. The tretament consists in avoiding the prolongation of labor by proper instrumental delivery without delay, and by applying a well-fitting bandage about the pelvis. In performing symphysiotomy or pubiotomy, care should be taken that at the moment of delivery the two halves of the pelvis are not rotated too widely asunder.

The Slow Pulse of the Puerperal Period.—Lynch (*Surg., Gyn., and Obstet.*, May, 1911) has investigated 105 cases to determine the lessening of the pulse rate after the birth of the child. These were 103 primiparæ and 82 multiparæ. Slowing of the pulse of multiparæ occurs twice as often as in primiparous patients, in whom the pulse beat is often unchanged in the puerperal period. In six out of every ten women in the series examined the average pulse was three or four

beats slower than normal. In the total series a fall of ten or more beats was observed in 20.5 per cent., in 31.7 per cent. of the multiparæ, but in 12.7 per cent. of the primiparous women. The more rapid the pulse has been during pregnancy, the more apt is it to be slower in the puerperal period. While the slower the pulse during gestation, the more apt is it to increase in rate after the birth of the child. In the majority of cases the pulse does not rise when the patient leaves her bed, about the eighth day.

The Relation of the Thyroid Gland to the Female Generative Organs.—Goodall and Conn (*Surg., Gyn., and Obstet.*, May, 1911) report cases illustrating this subject, demonstrating that a very intimate relationship exists between the female generative organs and the thyroid glands, this relationship being especially close between the thyroid and the ovaries. The uterus has no influence upon thyroid activity, except as it may affect the action of the ovaries. The function of the thyroid gland is, in a measure, under the control of ovarian activity, and when this is in excess, exophthalmic goitre often develops. When ovarian activity is diminished or absent, myxedema may result. Puberty, menstruation, pregnancy, lactation, and menopause all have a profound influence upon thyroid secretion. Thyroid and ovarian secretions neutralize each other, and the interstitial cells of the ovary are the important factors in producing this result.

The Beginning of Mind in the Newborn.—Peterson (*Bull. Lying-in Hosp. of N. Y.*, December, 1910) reports the results of investigations made in the New York Lying-in Hospital to determine the degree of mentality present in the newborn infant. From these studies he concludes that sensibility to light is present in most infants at birth, even when premature. The optic nerve is ready to receive impressions before birth. The same is true of hearing, as many normal children react to sound on the first day of life, and also a considerable number of those prematurely born. Children react to stimulation of the gustatory nerve at birth, and often before the period of normal gestation. This is also true of the olfactory nerve. There is every reason to believe that cutaneous sensibility, muscular sense, sense of motion, and of position are present, not only at birth, but for some time before. Thirst hunger is experienced on the first day, although hunger for food is not usually apparent until the first or second day. There are good reasons for believing that a newborn child comes into the world with a small store of experiences and appreciated feelings and shadowy consciousness. The child's body transmits light readily and must also transmit sound, and the child must have heard *in utero* the sound of the mother's body and also its own heart beat. The gustatory nerve is stimulated by swallowing amniotic fluid. Touch and muscular sense must be developed by fetal movements, which occur as early as the sixteenth week of pregnancy, and may be so violent as to give pain to the mother. Muscular activity and frequent contact of the fetal body with the uterine walls must develop a sense of equilibrium and relation to space. The material basis of consciousness is prepared long before birth. There is no perceptible difference in the reaction of colored and white or between twins.

GYNECOLOGY

UNDER THE CHARGE OF

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Study of the Structure of Myomata by Means of a Myoglia Stain.—Heimann (*Zentlbl. f. Gyn.*, 1911, xxxv, 701) believes that so little progress has been made in establishing a definite, characteristic structure for uterine myomata, owing to the fact that the ordinary stains used in their study, such as van Gieson, do not bring out the finer details of the muscle fibers. He calls attention to the occurrence in the smooth muscle cell of two kinds of fibrils, which according to Benda are to be considered as differentiation products of the cell body, as having, therefore, arisen from protoplasm. One set of these is finely fibrillar; they constitute the so-called "Binnenfibrillen," forming the mass of the cell body; the others, coarsely fibrillar, form the "Myoglia" of Benda, or the "Grenzfibrillen" of Heidenhain. These lie around the periphery of the cell, do not enter into it, but extend beyond the end of the cell and intertwine with corresponding fibrils of neighboring cells. By means of Benda's special myoglia stain, Heimann has found in a study of 25 small myomata, for the most part just visible to the naked eye, that in each case the muscle bundles radiate from a point, not necessarily anywhere near the centre of the tumor, which is sometimes formed by a lymph vessel, at others merely by a rich collection of muscle nuclei. He found even the smallest myomata to be made up of a number of these nodules, which structure can also be seen in quite large tumors.

Function of the Ovary.—In an article replete with references to the literature, as well as embodying original investigations, Frank (*Surg., Gyn., and Obst.*, 1911, xiii, 36) discusses the present status of our knowledge of the above subject. He calls attention to the fact that several glands in the body have a dual function, for example, the hypophysis has an anterior portion which is necessary to the maintainence of life, and a posterior or "nervous" portion, which is not so; the pancreas likewise has a double action. It furnishes an external secretion from the islands of Langerhans. It is not assuming a physiological curiosity, therefore, to consider that both the ovaries and testicles have an external secretion (ova, semen), and an internal secretion affecting the sexual life of the individual. The author considers the corpus luteum the most important constituent of the ovary in the latter respect, although in certain species of animals, but not in all, the existence of an "interstitial gland" has been demonstrated. He considers that the weight of evidence shows the corpus luteum to be developed entirely from the granulosa cells of the follicles; that it is therefore an epithelial structure. It has been shown by Loeb that the persistence of the corpus luteum is of the greatest importance in pre-

paring the uterus to receive the ovum, as without a corpus luteum in the ovary no decidua can be formed in the uterus; the fertilized ovum under these conditions merely acts as a foreign body in the uterus, and cannot obtain a foothold. When, however, the ovum is once firmly attached it becomes independent, and the removal of the ovaries or corpora lutea does not necessarily interrupt the pregnancy. The presence of a corpus luteum, moreover, lengthens the sexual cycle by absolutely inhibiting further ovulation as long as it persists; pregnancy *per se* does not do this, however, as if all corpora lutea are removed after pregnancy is once established, the remaining portions of the ovaries being allowed to remain in position, ovulation may occur. The factors causing the persistence of the corpora lutea in pregnancy are not known, but the author's investigations tend to indicate that neither the fetus nor the trophoblast are the sole factors.

Diagnosis of Renal Calculus.—Lichtenberg and Dietlen (*Münch. med. Woch.*, 1911, lviii, 1341) recommend for this purpose distending the pelvis of the kidney with oxygen, claiming several advantages for this method. Oxygen distends and renders röntgenologically visible the kidney pelvis and calices as well as does collargol, but it does not obscure the shadow of a stone as does the latter substance; it is therefore useful not only in diagnosticating the presence or absence of a stone, but also in showing its exact location, and whether it is best approachable by nephrotomy or by pyelotomy. The technique consists merely in introducing the ureteral catheter into the kidney pelvis, or high up into the ureter, and attaching its end to a tube from an ordinary oxygen tank such as is used for inhalation purposes. The pelvis becomes fully distended, the excess oxygen returning through the ureter alongside of the catheter to the bladder. The stream is kept running while the picture is being taken. No complications are to be apprehended, and the procedure is not painful.

Ovarian Transplantation.—Martin (*Surg., Gyn., and Obst.*, 1911, xiii, 53), as a result of a very extensive review of the literature of the subject, and of his own investigations, reaches the conclusion that autotransplantation (*i.e.*, transplantation of an ovary or portion of an ovary of an individual into the body of the same individual) is a comparatively simple procedure which may be accomplished, in the majority of cases successfully, by attaching the cut surface of the graft to any well-nourished tissue, such as the parietal peritoneum, abdominal musculature, subcutaneous tissue, etc. Even a very small portion of an ovary thus successfully grafted preserves the sexuality of the individual, and prevents symptoms of a premature menopause. Heterotransplantation, transplantation of an ovary from one individual into the body of another individual, on the other hand, succeeds much less frequently, owing to the antagonism of the blood of every individual to tissues of another, this antagonism not existing between the blood and tissues of the same individual. Martin suggests the possibility in the future of preparing patients in some way so as to render the blood and tissues of donor and recipient homogeneous, and thus make heterotransplantation more uniformly successful.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Beriberi.—FRASER and STANTON (*Philippine Jour. of Sci.*, 1910, v, 55 to 64) have carried out a series of experiments first upon chickens, then upon human beings, which indicate definite progress along both preventive and curative lines in beriberi. Chickens were fed upon unpolished and polished rice respectively. The chickens receiving polished rice, that is, rice containing no pericarp, developed a typical peripheral neuritis in from sixty to eighty days, while control chickens fed upon unpolished rice remained healthy. The experiments were repeated with similar results. The chickens showing symptoms of neuritis were then fed upon polished rice together with rice polishings, and in many instances fully recovered. Similarly those chickens which were fed upon whole rice and which remained well upon this diet developed polyneuritis when they were fed for a corresponding period upon polished rice. Apparently the process of polishing rice removes something which is necessary in order to maintain health upon a strict rice diet. The experiments were then carried out along similar lines upon human beings, and with the same general results; that is, that those individuals fed upon polished rice developed typical symptoms of beriberi, while those receiving unpolished rice remained well.

On the Etiology of Beriberi.—DEHAAN (*Ibid.*, pp. 65 to 71) has come to similar conclusions as follows: (1) *A* disease described as beriberi, or polyneuritis epidemica bears a very great resemblance in its etiology, prophylaxis, and therapeutics to the polyneuritis which can be artificially produced in animals, principally in fowls. (2) Just as is the case in the latter, the former is almost always the result of eating cleaned rice; that is, rice deprived of the whole of its pericarp, although other articles of food prepared in a similar manner may also cause an outbreak of the disease. (3) The pericarp of the rice and also some parts of the grain are removed in the manipulation by which unhusked rice becomes cleaned rice. Certain constituents of the greatest importance in securing normal nutriment for the peripheral nervous system are lost during this operation. (4) The constituents are neither salts nor nucleins, and (5) their character is still unknown.

Phosphorus Starvation with Special Reference to Beriberi.—HANS ARON (*Ibid.*, pp. 81 to 97) has studied the amount of phosphorus both in the polished and unpolished rice, and has carried out experi-

ments somewhat similar in nature to those just mentioned. His conclusions are: (1) Food stuffs, especially rice, which are relatively poor in phosphorus (phytim), if they are the main or exclusive article of diet for any great length of time, have been shown by various authors to cause beriberi. (2) The process of polishing removes the outer layers from the rice. These are rich in phosphorus, especially soluble organic compounds of that element (phytim). They are food constituents probably of high physiological importance. (3) A diet similar to that which is regarded as the probable cause of beriberi, if exclusively given for any length of time to animals, is not sufficient to keep them in normal health. (4) Polyneuritis has been observed in chickens receiving a food similar to that which is regarded as causing beriberi, viz., white rice. The addition of organic phosphorus in the form of phytim or its salts, considerably, but not entirely, produces a deleterious effect of a diet (white rice) which can produce polyneuritis in chickens.

Lead Poisoning in Illinois.—Alice Hamilton (*Jour. Amer. Med. Assoc.*, 1911, No. 61, pp. 1240 to 1244) calls attention to the unprogressive attitude of this country as compared with other countries, particularly those in Europe, concerning the recognition and dangers of lead poisoning. The lack of statistics and legislation in the United States for the control of the lead industries appears to be due largely to the fact that medical men have not taken the interest in the subject that the foreign medical men have, and this unprogressive attitude, it might be remarked parenthetically, is true for many other phases of the great question of occupational hygiene. The manufactures which employ the greatest number of men working in lead are those for white lead, lead smelting, the manufacture of storage batteries, printing establishments, and to a lesser extent those places where lead glazing is done. While it is well known that women are much more susceptible to lead poisoning than men, the statistics of Illinois indicate that very few women are employed in lead industries. The prevention of lead poisoning necessitates a campaign of education among those employed in the lead industries, the study of the conditions by competent investigators, the collection of statistics and presentation of statistics to legislative bodies, together with recommendations for the drafting of suitable laws regulating the manufacture of lead in factories.

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ORIGINAL ARTICLES

THE SPECIFICITY, DANGER, AND ACCURACY OF THE TUBERCULIN TESTS.[1]

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During the past ten years a great change of opinion has taken place in regard to the tuberculin test. The subcutaneous test with its disagreeable reaction has deterred many from using tuberculin diagnostically, and not until von Pirquet described his cutaneous modification and Wolff-Eisner and Calmette their conjunctival test, has tuberculin been universally used. These and other modifications have greatly extended our knowledge of this subject and it has seemed fitting at this time to review briefly my experience with tuberculin used for diagnosis and to draw whatever conclusion about its value that seem warranted.

1. The Specificity of Tuberculin. However it may be with diseases not transmissible to the ordinary laboratory animals, certainly among these animals only those react to the tuberculin tests which are tuberculous. Tuberculin, as Citron and others have shown, is not an ordinary toxin. Normal animals have tuberculin tolerance but no tuberculin anaphylaxis; tuberculous animals have tuberculin anaphylaxis and acquire tuberculin tolerance when properly treated with tuberculin. Normal animals may acquire anaphylaxis after injection of tuberculin when the second dose is

[1] Read before the Association of American Physicians, May 9–10, 1911.

given intravenously or intracerebrally, but Baldwin and Krause have been unable to produce any sensitiveness to tuberculin in normal guinea-pigs when the second dose is given cutaneously, intracutaneously, subcutaneously, or in the conjunctiva. This suggests that some difference exists between the mechanism involved in the ordinary tuberculin test and that concerned in anaphylaxis, though the difference is probably one only of degree. In Koch's first paper he called attention to the fact that it required 250 mg. to make him react, and in 1891 and again last year, reports have been published showing that infants, apparently healthy, fail to react to very large doses, even 1000 mg. repeatedly given. This simply bears out the experimental fact that only animals infected with tubercle bacilli react.

Many autopsy reports throw grave doubt upon, and personally, I believe, disprove all published statistics which go to show that other diseases (particularly syphilis) react specificially to tuberculin, but indicate that they are in reality instances of double infection. The cutaneous test has shown that patients with these diseases react to tuberculin in about the same proportion as ordinary individuals in poor health. That a slight tuberculous infection may be sufficient to cause reaction for a time and yet leave no permanent pathological change visible to the naked eye, is readily possible.

Leprosy, however, must be considered separately, for the interesting work of Babes suggests that while most of the lepers who react to tuberculin are tuberculous as well, still it is impossible in some to find any evidence of it clinically or at autopsy, and the reddening of the leprous nodules three days after the injection of tuberculin is of considerable interest. The reaction, he believes, is specific for leprosy in that it begins later (twenty-four hours) and lasts longer (for several days) than in the tuberculous, possibly not reaching its maximum until the third or fourth day. The cutaneous test is often absent, while in 50 per cent. of Babes' cases the conjunctival test was positive. Leprosy and tuberculosis are rarely confused, and the presence of lepra bacilli in numbers in the nasal discharge is of great aid in differentiation.

Recent work has tended to show that sensitiveness to the tuberculin tests cannot be produced in healthy individuals. This does away with any fear of a too slow increment of dosage and permits one to use and to draw diagnostic conclusions from a clinical course of tuberculin treatment. A slight reaction to a small dose at any time during the course of treatment would be proof sufficient that the patient had had a tuberculous infection.

2. The Danger of Tuberculin.—The conjunctival test has produced a number of unfortunate accidents, one of which, a central corneal opacity, came under my observation after the administration of the test dose. When the subcutaneous test follows a

positive conjunctival test, the eye may react again, or even during tuberculin treatment there may be for a time slight reddening. These objections, with the exception of the injury to sight, are of small moment and when carefully given, excluding all patients who have ever had the slightest trouble with their eyes and using only 1 and 5 per cent. solutions of the old tuberculin, the test seems comparatively safe. General reactions have followed its use, and on the whole it should be avoided in children.

The cutaneous test has produced lymphangitis, extending from the forearm to the elbow or even the shoulder, with slight swelling of the lymphatic glands in several instances, and in another case rather extensive ecchymosis but no necrosis. Several general reactions have occurred in my patients. Certainly the dangers of the cutaneous test are so slight as to warrant no consideration except in scrofulous children.

The subcutaneous test to be positive demands a general reaction, and anyone who has experienced a severe reaction to tuberculin will agree with me that the ordeal is, to say the least, decidedly unpleasant. In the majority of patients the only symptom remaining at the end of the second or third day is a little weakness, which is speedily replaced in many instances by a feeling of improvement. I have repeatedly been asked on this account by these patients for permission to take tuberculin therapeutically. On the other hand, in a few instances, I have seen a slight temperature persist for months after a subcutaneous test when it had been normal previously. In one case expectoration, which had been absent before, was present for two or three years afterward, but it is no uncommon thing for patients who have never had tuberculin to present similar histories. In several instances, on the other hand, patients to whom we were about to administer tuberculin, but for some reason failed to do so, had attacks of pleurisy, hemiplegia, etc.

The discovery for the first time of tubercle bacilli in the sputum just after a subcutaneous tuberculin test, often only indicates that the sputum had not been examined frequently enough before the test. Without doubt tubercle bacilli are present in the sputum of many patients when, after one or two ordinary examinations, they are stated to be absent. In one instance we gave 0.2 and 1 mg. to a patient with negative sputum without reaction of any sort and then found tubercle bacilli in the sputum, which had again become slightly blood-streaked. In another apparently doubtful case, while we were considering the use of the tuberculin test, we found tubercle bacilli in the sputum.

The occurrence of tubercle bacilli in the sputum following or after this test has long been held as proof of the lytic activity which many assume to occur during this reaction. In the 286 tests under

consideration, tubercle bacilli were found in the sputum subsequent to the test in 18, fourteen times in the incipient and four in the moderately advanced cases. In order to connect the test with the occurrence of tubercle bacilli as cause and effect, we must establish some limit of time in which the tubercle bacilli must occur. I have arbitrarily chosen two months, but in most instances all effects of the reaction have passed in two or three days. Of these 18 cases, 5 incipient and 2 moderately advanced occurred within this period, 4 within one and 3 within two months. In one instance included here, the test was negative, in another tubercle bacilli were found before a single subcutaneous dose was given while in a third the test was given while the patient was waiting admittance and before the sputum was subjected to as prolonged search as afterward. If we exclude these 3, the figures would indicate that tubercle bacilli are two or three times as likely to occur after as within the time limit of two months. When it is considered that tubercle bacilli occurred after the test in only 6 per cent. of 286 cases, and that in less than 2 per cent. did there occur bacilli within two months after the test, it seems that little weight can be attached to the tuberculin test as the cause of the occurrence of tubercle bacilli in the sputum. If the occurrence of tubercle bacilli in the sputum after the subcutaneous test was connected with the test it is only reasonable to expect to find some signs of congestion and softening in patients whose sputum later showed the presence of tubercle bacilli. In only 2 of the 18 cases previously mentioned were the respiratory symptoms increased, 1 of which was the instance where there was only an intradermic test. In all, 40 patients showed some increase of the respiratory symptoms, and in only 1 could the reaction be considered in any way connected with the occurrence of tubercle bacilli in the sputum. My experience, therefore, leads me to believe that any apparent connection is due entirely to coincidence.

At the Adirondack Cottage Sanitarium, our routine has been to require all patients who have never had tubercle bacilli in their sputum to undergo the subcutaneous test. More recently I have come to hesitate about giving it. When a patient is doing well it is a curious thing that very little seems required to upset the balance and turn, for a time at least, the scale against him. The greatest danger that I have seen result from the subcutaneous test is such a slight temporary disturbance; but without doubt, more danger, however slight, is connected with this test than with the cutaneous or intradermic tests.

3. The Focal Reaction in the Lungs. An increase of physical signs occurred in the lungs in 39 per cent. of 127 patients who were carefully examined, during the reaction and for the most part two days later, or if we include 17 doubtful cases in 45 per cent.

The occurrence of this so-called focal reaction seems to be little connected with the severity of the reaction as manifested either by the symptoms or by the degree of temperature. Symptoms referable to the respiratory tract seem to occur with about equal frequency in those with and in those without increase of physical signs. These respiratory symptoms, however, were in almost every case connected with marked general symptoms, but apparently occurred independently of the degree of fever and showed very little tendency to occur more frequently in early stages of the disease. In a few cases the increased physical signs, persisted, and it is possible that in these and in a few others they were overlooked at the first examination.

4. The Value of the Tuberculin Test. A test, to be of real value, should enable us to differentiate not only tuberculosis from other diseases, but also clinical tuberculosis from non-clinical tuberculosis. The latter I define as an infection with tubercle bacilli, which has not reached a stage in which it can be diagnosticated clinically, while the definition of "clinical tuberculosis" is self-evident. Clinical tuberculosis may be masked, active, quiescent, or arrested, stages which can be separated only by the symptoms and physical signs which the patient presents, or by the lack of them.

The occurrence of a tuberculin reaction in apparently healthy men is an interesting phenomenon which would occur probably in a large percentage of middle-aged individuals. It varies, as Franz has shown, more or less directly with the incidence of tuberculosis in the race. It possesses in health no clinical importance, If, however, these same healthy men later fall ill of non-tuberculous diseases, what is going to prevent their reacting, in part at least, to tuberculin? Nägeli's figures and Franz's statistics both warn us of the danger of depending too much upon this test.

In my experience at the Adirondack Cottage Sanitarium, where for several years all patients without tubercle bacilli in the sputum have been required to undergo the subcutaneous test as a routine measure, I have come to believe that failure to react to 10 mg. of old tuberculin, given subcutaneously, does not exclude clinical tuberculosis. However, in the presence of indefinite symptoms, it indicates that in all probability, treatment is unnecessary. I have allowed these patients to return home at once, and so far no doubtful clinical case, which has failed to react to 10 mg. has relapsed, after one to six years, though we have had only 12 such cases. Nine other cases reacted first to 10 mg. One patient who failed to react to 6 mg. was classified as doubtful for several years, but finally relapsed, had tubercle bacilli in his sputum, and tuberculous cervical glands.

I have no doubt that some patients who react to doses much

smaller than 10 mg. may suffer only from tuberculous infection, and that the symptoms they present may be due to causes other than tuberculosis. Over one-half (52 per cent.) of our advanced cases reacted to 1 mg. or less, while considerably less than half of the incipient cases (42 per cent.) reacted to the same dose. In only 4 per cent. of the advanced and 15 per cent. of the incipient cases was it necessary to give over 5 mg. to produce reaction. A negative subcutaneous test in a tuberculous patient may indicate either the absence of receptors at the site of the lesion or the presence of free antibodies in the blood. In a certain number of these cases complement deviating substances (amboceptors) have been found in the blood, and in the patient whose clinical history and physical signs point strongly to a diagnosis of tuberculosis, the occurrence of these substances may explain the negative subcutaneous test.

Healthy infants do not react to 1000 mg. Some patients with clinical tuberculosis react only to 10 or more milligrams. There is, therefore, no known limit at which a healthy man will react and no known limit which divides patients with tuberculous infection from those with clinical tuberculosis. Certainly, failure to react to 10 mg. or less does not surely disprove the presence of clinical tuberculosis. Of 9 patients, who failed to react to 10 mg. given subcutaneously, 4 reacted to the cutaneous test, while 3 failed to do so to old tuberculin in full strength, and 2 showed a positive local reaction (Stickreaktion). One of the 3 patients with a negative cutaneous reaction reacted to the intradermic test. The local reaction was positive in every instance (176) where it was noted in patients who reacted to the subcutaneous test.

The cutaneous test is of value in early life, though when its reliability ceases is difficult to determine. Certainly, after seven or eight years, a positive reaction is of little value, for by this time tuberculous infection and clinical tuberculosis are vastly different things, and without doubt the great majority of both react to the cutaneous test. I cannot yet accept a negative skin reaction as excluding either tuberculous infection or clinical tuberculosis, as I know of tuberculous patients in good condition who have failed to react to old tuberculin in full strength. This absence of reaction of the skin or conjunctiva may indicate only that no sessile receptors are present in these parts, not that the patient is without tuberculous infection. Many attempts have been made by graduating the dose in the cutaneous test, to separate clinical tuberculosis from tuberculous infection. Ellerman and Erlandsen believe that they have accomplished this, and suggest the use of a rather complicated formula based upon the differences of the average diameters of the papules when four scarifications have been made through four simultaneously applied doses of tuberculin, each four times stronger than the preceding, for example, 0.5 per cent., 2 per cent., 8 per

cent. and 32 per cent. O. T. Some have not been able to verify the work of Ellerman and Erlandsen, nor has it been proved, providing a sufficient amount be used, that the quantity of the solutions plays a very important part. My experience leads me to believe that the more nearly the technique approaches that used for vaccinia, the more reliable the results. In any individual patient, if he react to one drop of 1 per cent. or of a 5 per cent. solution of old tuberculin given in different eyes, he is more likely to have clinical tuberculosis than if he reacted only to the cutaneous test.

The intradermic test should, theoretically, be far more accurate than either the conjunctival or the cutaneous test, however applied, for all the tuberculin given reaches the interior of the skin. It admits further of accurate dosage which, on account of the possible variation in power of absorption of the skin and the difficulty of keeping all the solution over the abrasion or in the conjunctiva until absorbed, is impossible in either the cutaneous or the conjunctival tests. In some instances certainly it is more sensitive than the skin test, reacting where the latter is absent. While a dose of 0.02 of a milligram has never caused a general reaction, we have no record of any patient failing to react to this dose given intradermically.

In brief, if we except for the time being, leprosy, tuberculin is a specific test for the detection of tuberculous infection. The danger from the use of the tuberculin test is slight, but in some unsuitable cases very real and possibly severe. Reaction, even when severe, has no connection with the appearance of tubercle bacilli in the sputum. Increase of physical signs occurs in about one-third of all the cases and in one-half of those with increase of pulmonary symptoms and is independent of the appearance of tubercle bacilli in the sputum. In practice, exposure to infection, characteristic symptoms, such as hemoptysis, pleurisy with effusion, dry pleurisy on both sides, and localized persistent physical signs at one apex, are diagnostic data of far more importance in clinical tuberculosis than that derived from the tuberculin tests. A positive reaction, when only doubtful symptoms of pulmonary tuberculosis are present, is of uncertain value unless the pulmonary symptoms or signs are definitely increased during the reaction. A negative reaction is of uncertain value, and in the face of positive symptoms carries little weight. In many instances the tuberculin tests add only confusion to the clinical data. The subcutaneous test, depending as it does upon the reaction at the site of the lesion, is still today the most reliable of the tuberculin tests; but neither this nor any of the modifications as yet devised, differentiate clearly clinical tuberculosis that demands vigorous treatment from non-clinical tuberculosis that requires only a God-fearing life.

TUBERCULOUS INFECTIONS CLASSIFIED FOR AID IN DIAGNOSIS AND TREATMENT.

A. Diagnosis.

I. Non-clinical tuberculosis.
No symptoms or physical signs.
May or may not react to tuberculin tests.
II. Clinical tuberculosis.
With symptoms or physical signs or both.
Usually react to tuberculin tests.
(*a*) Masked.
Physical signs only, no symptoms.
(*b*) Active.
Symptoms present.
Physical signs usually present.
(*c*) Quiescent or arrested.
Symptoms present now or formerly.
Physical signs present or absent.

B. Treatment.

A. Not necessary.
I. Non-clinical tuberculosis.
II. Clinical tuberculosis.
(*a*) Masked.
B. Necessary now or formerly.
II. Clinical tuberculosis.
(*b*) Active.
(*c*) Quiescent or arrested.

IS PERNICIOUS ANEMIA OF INFECTIOUS ORIGIN?[1]

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Since Addison's description, various types of anemia due to carcinoma, sepsis, parasites, etc., have been differentiated, but there is still left a large group of cases for which the title of cryptogenetic pernicious anemia must be preserved. No matter where

[1] Read before the Association of American Physicians, May 10, 1911.

seen—in Austria, Switzerland, Germany, Paris, London, Boston, or California—these cases are symptomatically remarkably alike. The difficulties of distinguishing the characteristic blood changes from so-called secondary anemias seem to me much exaggerated. Clinically, the general appearance of the patient, the fever, the cardiovascular, gastro-intestinal, and nervous symptoms, the peculiar remissions, pathologically the pronounced fatty degenerations, the siderosis in liver, spleen, and kidneys, the marrow changes, are as characteristic of the disease as the blood picture. The constancy of these phenomena in practically all cases is in favor of a definite clinical entity, the result of some specific intoxication.

Nearly all authors now agree that the marrow changes are secondary, represent regenerative efforts, and are not in any way specific. Recent investigations have been concerned chiefly with causes of the pathological hemolysis, which is a main feature of the disease. Experimentally by injection of toluylendiamine, ricin, pyridin, saponin, hemolysis may readily be induced and marrow changes and a blood picture may result that closely resemble those of pernicious anemia. Schaumann, Faust, and Tallquist have shown that the anemia due to bothriocephalus is the result of hemolysis produced by a lipoid substance that may be extracted from the segments. In these cases, also, lipoid bodies are to be found in increased amounts in the gastro-intestinal tract. The hemolytic substance isolated by Tallquist was either the sodium or cholesterin combination with oleic acid; normally but little cholesterin was to be found in blood, and when a certain concentration was reached hemolysis occurred. Tallquist suggested therapeutically calcium salts or glycerin to form insoluble or harmless compounds with oleic acid. On the other hand, von Eisler, following the observation of Kruskal that serum inhibited to a certain degree the hemolytic action of saponin, showed that this was due to cholesterin, and Ransome demonstrated that the specific resistance of the erythrocytes was likewise dependent upon cholesterin. In animals, the resistance to saponin hemolysis runs parallel with the cholesterin content of the serum. Morgenroth and Reicher, working with cobra venom and other toxic lecithins, proposed the use of cholesterin therapeutically to inhibit hemolysis. Fejes has recently written of anemia produced experimentally by bacterial hemolysins. Berger and Tsachiya extracted a lipoid substance from the intestinal mucous membrane of individuals dying from pernicious anemia, and found its hemolytic action ten times more potent than extracts from other cases. Anemia of the pernicious type resulted from its injection in animals, a similar lipoid could be obtained from the gastro-intestinal mucous membrane of dogs after production of moderate inflammatory changes. Schlaepfer, employing the method of Ciaccio for preserving lipoids, found lipoid bodies in the intestinal mucous membrane of two cases of pernicious anemia;

in a normal intestine and in a case of secondary anemia they were not obtained. The reports about the various lipoids are, however, still conflicting; other observers have extracted hemolytic substances from the normal intestine, so that we must conclude that no specific toxic body has yet been found.

The recent paper of Grawitz advocates anew the theory of gastro-intestinal intoxication and lays particular stress upon the absence of hydrochloric acid in the stomach as an important factor. But achylia may exist for years without anemia, it is associated not infrequently with intestinal parasites—tenia, uncinariasis, amebiasis—and may result from malignant disease in any part of the body. It is a symptom and not a cause of pernicious anemia. The writer has seen several cases treated by the Grawitz method progress steadily to a fatal issue. Witherspoon has reported a number of cases apparently benefited by measures directed toward the gastro-intestinal tract. In one instance, the symptoms and the character of the stools were influenced favorably by appendicostomy and irrigation. Favorable results have followed the administration of lactic acid preparations. Grawitz would interdict animal albumin in the diet, while Strauss and others advocate overfeeding with meat and peptones. The absence in the majority of cases of signs of intestinal putrefaction, the remarkable appetite and digestion exhibited by many patients, the improvement and apparent cure that may occur without any treatment whatsoever, the persistence of the achylia during remissions—these fact are decidedly against a primary gastro-intestinal intoxication as a cause of the disease. The crises of vomiting and diarrhea not infrequently observed resemble closely the attacks in the course of exophthalmic goitre. Improvement of all symptoms and of the blood picture may follow such a crisis and suggests the elimination of toxic products or the destruction of great numbers of parasites.

Comparatively little has been done in searching for an infectious cause of pernicious anemia. Swiss authors have dwelt upon the occasional endemic occurrence. In the past year, I have seen 7 cases from one of the large interior valleys of California, 3 being from a town of 10,000 inhabitants. Rarely the disease has been observed in two or more members of a family. Of interest in connection with the pernicious anemia of horses, later to be described, is the opinion of some foreign authors that the affection is more commonly met with in country districts. Of 25 cases seen by the author in the past two years, only ten were in city dwellers. The statistics of Cabot, however, by far the best at our command, show that place of residence and condition of life have no influence in etiology.

The theory of buccal or gastro-intestinal infection advanced by Hunter, has been generally abandoned—the sore mouth, not infrequently seen is a symptom and not a cause of the disease. Von

Jacksch, and more recently G. Klemperer have suggested a protozoal origin. Hoefer in a case with recurring fever once, during a period of temperature, observed some peculiar bodies both within and outside the red corpuscles. They resembled piroplasma, but were larger; culture and animal experiments were negative.

Many points of similarity between trypanosomiasis or piroplasmosis and pernicious anemia suggest the possibility of a protozoal infection.

1. Anemia is a prominent feature in many forms of trypanosomiasis and in piroplasmosis—in surra, dourine, caderas, galziekte. In kala azar anemia is usually moderate, but Sheka and Zoypfl have reported the case of a boy, aged nine years, with a count of 2,400,000 red and 1100 to 2000 white cells. In infantile splenic anemia, the result of infection with Leishmania infantum, very low counts have been recorded. In Texas fever in cattle when organisms appear in the peripheral blood, sixty to eighty days after the infecting tick bite, anemia gradually becomes apparent, anisocytosis, poikilocytosis, polychromatophilia, basophilia occur, and normoblasts and megaloblasts later appear. Leukopenia, relative lymphocytosis, and a high color index usually are feature of these protozoal infections.

2. Fever occurs in 79 per cent. of the cases of pernicious anemia (Cabot). Its frequency speaks against a purely toxic cause. It may continue for weeks, may recur periodically, or may be absent during long remissions. Similar peculiarities of the temperature are observed in trypanosomiasis. In certain instances of pernicious anemia, high temperature, profound exhaustion, marked nervous symptoms, and a considerably enlarged spleen speak strongly in favor of a rapidly progressing infection.

3. The remissions of pernicious anemia are among the most remarkable features of the disease; similar remissions are characteristic of a number of protozoal infections. The recurrence of all clinical phenomena of the disease and progression to a fatal issue after remissions of five, ten, fifteen, and even twenty years, make one hesitate to speak of cures in pernicious anemia. Todd, in a recent paper, has emphasized the long periods of apparent freedom in human and animal trypanosomiasis, five and eight years before a final relapse proves fatal.

4. The nervous symptoms and lesions of pernicious anemia, syphilis, and trypanosomiasis are, as Mott and other have pointed out, decidedly similar. But little work has yet been done on the cerebrospinal fluid in cases of pernicious anemia with cord symptoms. In two cases I have found a moderate increase of small mononuclear cells and a positive Nonne, but no Noguchi reaction. These cases, as well as two others without spinal fluid examinations gave a negative Wassermann.

5. From recent investigations, certain lipoid substances seem to play a role in hemolysis in pernicious anemia. Lipoid bodies are likewise increased in syphilis, a spirillosis, and in trypanosomiasis.

6. The only remedies of any value in pernicious anemia are arsenic and arsenical combinations, and arsenical compounds have been found a specific in syphilis and in some forms of trypanosomiasis.

The affection known as equine pernicious or infectious anemia has, of late years, been thoroughly investigated by Carré and Vallée in France, and by Ostertag, in Germany. The first-named authors succeeded in transmitting the disease by inoculation of blood intravenously and subcutaneously and by feeding blood and urine of infected animals. They found the virus potent even after passage through bacterial filters. It is questionable whether the American swamp fever is the same disease. Four years ago, cases of pernicious anemia were noted among horses in one of the interior valleys of Washington, and I am indebted to W. B. Mack, of the University of Nevada, for published reports and recent accounts of cases occurring in eastern Nevada. For fifteen or twenty years, fatalities have been noted among the horses in certain districts, and in 1906 and 1907 the disease became epidemic, causing the death of all horses on some of the ranches. Since 1907, there have been scattered cases. All ages and conditions have been attacked, the disease running an acute, subacute, and chronic course. Few animals recover, though there may be long remissions and apparent cure. The symptoms of subacute and chronic cases are very similar to those of pernicious anemia in man. Irregular high temperatures may persist for weeks or months. Progressive weakness and anemia, throbbing of the vessels of the neck, cardiac insufficiency, dyspnea, edema, paralysis of the hind extremities are the chief symptoms. The appetite is usually ravenous; enlargement of the lymphatic glands may occur. The normal blood count of horses at the altitudes involved in Nevada, about 6000 feet, is given by Mack as considerably over 8,000,000. The lowest count recorded was 2,120,000, with 7300 leukocytes and 38 per cent. hemoglobin. There is always a leukopenia in uncomplicated cases with a relative lymphocytosis—the color index is high. Macrocytosis and nucleated red cells have been observed, but Mack comments upon the fact that the changes in the erythrocytes are not as great as would be expected from the degree of anemia. The disease may be characterized by remissions exactly similar to those that occur in pernicious anemia in man.

Autopsies on fatal cases have shown extensive subserous hemorrhages, fluid in the serous cavities, spleens sometimes normal in size and again considerably enlarged. Extensive megaloblastic metaplasia of the bone marrow has been a constant feature. In two instances, in 1907, Mack succeeded in transmitting the disease to

other horses by subcutaneous injection of defibrinated blood from diseased animals. The clinical symptoms, remissions, and autopsy findings were the same as in other cases. His recent experiments have been less positive, and he writes under date of April 19, 1911: "I have been unable to find any microörganism associated with the disease which can be regarded as the causal factor. I have searched diligently for such an organism; bacteria frequently occur in the tissues, but they do not cause the disease; piroplasma or other protozoa have not been found. Some investigators consider the cause a filterable virus, but I have not demonstrated that in my cases; in fact, my inoculations have yielded somewhat conflicting and puzzling results."

During the last year several of my cases have been investigated with the idea of a protozoal origin in mind. Films have been stained or preparations made after the method of Martin and Leboef,[2] centrifugalizing 5 c.c. of blood from a vein to which 1 c.c. of 20 per cent. sodium citrate in normal salt solution has been added. Cultures have been attempted both in normal salt solution recommended by Nuttall and in the 2 per cent. citrate of sodium solution of Rogers, and on the medium advocated by Novy. No bodies resembling protozoa have been found. Inoculations in guinea-pigs have been made, using 2 to 3 c.c. of blood, with negative result. Very few inoculation experiments have been reported in human pernicious anemia. I have in mind in future inoculations of large amounts of blood, of blood from splenic puncture, and of extracts of the tissue at autopsy into dogs, monkeys, and horses. The cases most likely to give positive results are those rather rare ones marked by a rapid progressive course, high temperature, and a greatly enlarged spleen.

THE COAGULATION TIME OF THE BLOOD IN VARIOUS DISEASES.[1]

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The method of estimating the coagulation time of the blood, as described by one of us (R. D. R.) last spring before the Association

[2] Diagnostic microscopique de la trypanosomiase humaine, Ann. de l'Inst. Pasteur, 25 Juni, 1908, I, xxii, No. 6, pp. 118 to 540.

[1] Read by title before the Association of American Physicians, May 10, 1911.

of American Physicians, has been considerably used during the past winter in the wards of the Toronto General Hospital and to a less extent in the Sick Children's Hospital here. The routine work was carried out almost entirely by one of us (C. E. C. C.).

The instrument employed has proved to be a convenient one clinically, being both portable and easily manipulated.

As was pointed out when the method was first described, the results obtained by this or by any other apparatus are in no way absolute, but merely denote the coagulation time of a given blood, *in vitro*, at a given temperature. At 20° C., the temperature at which all the work was done, the average clotting time in health is about seven minutes; but the time may vary considerably from the average in normal people, just as do pulses, blood pressures, etc.

The firmness of the clot may be gauged roughly at the time of the test, but of course, cannot be expressed in figures, as the clotting time may be. This firmness of the coagulum is a very important matter, and upon it probably depends the stopping of a hemorrhage as much as it does upon the mere fact of clotting having occurred.

The results here given are too few to be of any great value, but some interesting points have come out, and moreover, as others are working with the same apparatus, in time, su ficient data may be collected to give the range of clotting in different conditions. Some 300 tests were made of the blood of about 150 patients, with the results shown in the accompanying table.

Remarks. *Secondary Anemias.* Secondary anemias other than those due directly to hemorrhage, appeared to have a normal clotting time. Twelve observations were made upon 6 patients, with an average clotting time of 7.8 minutes, and a range of from 10.5 to 6.4 minutes. When the anemia resulted from hemorrhage, the clotting time was invariably shortened, except in the case of hemophilia, when hemorrhage appeared to have no such effect. In 8 cases of hemorrhage, with 14 observations, the average clotting time was 6.6 minutes, with a range of from 5.2 to 10 minutes. The one that showed a time of 10 minutes was a case of epistaxis in an old woman. It was not severe, but was very persistent and hard to control. There was no history in the family of bleeding nor of previous hemorrhages. In 1 case of severe traumatic hemorrhage the clotting time was 6.4 minutes. The patient was then transfused by Crile's direct method, and afterward the clotting time was practically the same (6.5 minutes). The donor, his brother, showed before the transfusion a clotting time of 8.5 minutes, and directly after one of 5.8 minutes.

Antitoxin. Some 6 healthy children were tested before and after the administration of a prophylactic dose of antitoxin. The dose given was always 500 units, which bulks about 3 c.c. There was no change produced in the clotting time.

Disease.	Number of patients.	Number of observations.	Average clotting time in minutes.	Maximum clotting time in minutes.	Minimum clotting time in minutes.	Remarks.
Acromegaly	1	5	9.4	10.4	9.0	
Addison's disease	1	4	9.3	9.7	8.9	
Anemia: (*a*) Secondary:						
(1) Not due to hemorrhage	6	12	7.8	10.5	6.4	See remarks.
(2) Due to hemorrhage	8	14	6.6	10.0	5.2	See remarks.
(*b*) Pernicious	4	8	6.7	7.4	5.2	
Aneurysm	1	5	9.4	10.7	7.0	
Antitoxin to healthy people	6	12	....	....	....	See remarks.
Appendicular abscess	1	2	9.0			
Arteriosclerosis	1	2	7.4	7.6	7.0	
Chlorosis	2	4	6.9	8.0	6.2	
Chorea	1	1	7.7			
Dermatitis exfoliata	1	2	6.5	7.0	6.0	
Diabetes insipidus	1	2	11.5	12.2	11.2	
Diabetes mellitus	3	6	7.0	8.0	5.6	
Goitre, exophthalmic	4	9	7.5	8.5	6.2	
Goitre, simple	1	2	7.2	7.2	7.2	
Eczema seborrhoicum	1	2	6.6	6.8	6.4	
Empyema	1	2	6.5	6.6	6.4	
Erysipelas	3	5	9.2	10.8	6.5	
Gastric neurosis	2	4	8.1	8.5	7.5	
Gastric ulcer	3	6	6.8	7.7	6.2	
Hemophilia	2	10	14.25	20.0	9.5	See remarks.
Heart-block	1	3	7.1	7.6	6.7	
Influenza	1	1	7.7			
Jaundice	6	10	9.6	12.0	6.5	See remarks.
Leukemia, splenomyelogenous	1	5	8.1	9.5	6.2	See remarks.
Meningitis (pneumococcic)	1	2	4.6	5.2	4.0	
Nephritis (chronic)	3	6	8.2	10.1	8.1	
Neurasthenia	1	1	7.7			
Polycythemia	1	3	10.1	10.7	9.5	
Purpura	3	8	6.2	7.6	4.9	See remarks.
Raynaud's disease	1	2	6.6	6.8	6.5	
Renal colic	1	2	8.2	8.5	8.0	
Rheumatic fever	15	38	10.2	14.3	7.0	See remarks.
Rheumatoid arthritis	1	2	6.8	7.0	6.6	
Pneumonia, broncho-	1	4	9.9	10.5	9.2	
Pneumonia, lobar	17	47	8.1	12.7	5.5	See remarks.
Septicemia	4	8	8.3	9.7	7.4	
Tuberculosis, various forms	9	18	8.9	10.4	7.0	
Typhoid fever	26	60	7.1	12.0	5.0	See remarks.
Urticaria	1	2	8.1	8.5	7.7	

Hemophilia. Two cases, both typical as regards the family tendency to hemorrhage, etc., showed very different readings as regards their time of coagulation—one giving an average of 9.5 minutes and the other one of 19 minutes. The one that showed the greater delay was given calcium lactate freely for two days, 30 grains every four hours, with a sequence of a clotting time of 20 minutes. A few days later he was given 15 c.c. of rabbit blood serum

subcutaneously without any perceptible effect upon the clotting time.

Jaundice. Six cases of jaundice showed an average clotting time of 9.6 minutes as a result of ten observations. The minimum time was 6.5 and the maximum 12 minutes. In none of them had there been any recent hemorrhage.

Splenomyelogenous Leukemia. A case of this disease, which remarkably improved as regards the blood picture under the bi-weekly use of *x*-rays, showed the following clotting times in relation to the white cell count: When the leukocytes were 300,000 the clotting time was 6.2 minutes; when the leukocytes were 130,000 the clotting time was 8.6 minutes; when the leukocytes were 12,000 the clotting time was 7.6 minutes; when the leukocytes were 2000 (*x*-rays stopped) the clotting time was 9.5 minutes; when the leukocytes were 2200 the clotting time was 8.5 minutes. Thus, the clotting time here showed some lengthening as the leukocytes dropped in number.

Lobar Pneumonia. Forty-seven observations were made upon 17 cases of this disease, and the average clotting time was 8.1 minutes, but ranged from 5.5. to 12.75 minutes. The clotting time did not vary with the acuteness of the infection, 2 fatal cases showing a time of 8.25 and 8.75 respectively shortly before death. No marked daily variations occurred, but 1 case that was followed daily showed a tendency to hastening of the coagulation time until the crisis, when it swung back to normal. Thus, on the fourth day the clotting time was 8.75; on the fifth day, 8.5; on the sixth day, 8.2; on the seventh day, 7.5; on the eighth day (critical), 6; on the ninth day, 7.3, and on the tenth day, 7.6 minutes.

Purpura. Three cases of this condition, in which subcutaneous hemorrhages occurred without definite cause, showed an average coagulation time of 6.16 minutes from eight observations, the range being from 4.9 to 7 minutes. Thus the clotting time in these cases seems to be rather hastened than otherwise.

Acute Rheumatism. Thirty-eight observations were made upon the blood of 15 cases of this disease, and the average clotting time was found to be 10.2 minutes, with a range of from 7 to 14.3 minutes. Thus, the clotting time in acute rheumatism seems to be lengthened. It was noted that the clotting was delayed as long as the acute pain lasted, but it did not seem to have any special relation to the degree of fever present. All these patients were freely treated with salicylates, but the delay in the clotting time was not due to this medication, as in several of the cases the first estimates were before the remedy was commenced, and in most of them the drug was still being given after the pains had ceased and the coagulation time had consequently become faster. Thus, in one of the cases the coagulation time was 14.3 minutes before any medicine had been given, and when the pain had disappeared, the time had shortened to

eight minutes, and yet the salicylates had not been discontinued. In two of the cases calcium lactate was given in 30 grain doses every four hours for two days without the clotting time being at all shortened. One case was complicated with pericarditis and another with quinsy, without any apparent effect upon the coagulation time.

Typhoid Fever. Sixty observations were made upon 26 cases of this disease, and the average clotting time was found to be 7.1 minutes, with a range of from 5 to 12 minutes. Two cases, which had phlebitis, and had been treated for four and seven days respectively, with large doses of citric acid (30 grains every four hours), showed a coagulation time of 5.3 and 7.1 minutes; 1 case showed a shortening in the clotting time of from 7.5 to 6.25 minutes following three days of profuse diarrhea. The severity of the invasion did not seem to have any effect upon the clotting time.

Conclusions. 1. The instrument used is a convenient one for clinical purposes, and gives, with constant technique, fairly constant results. Thus, if the coagulation time of an individual be estimated several times within a few minutes of each other the readings will seldom differ by more than a minute, and are usually within half that time of one another.

2. Coagulation time, as estimated *in vitro*, and a tendency to hemorrhage are not necessarily related to each other. Thus, a patient may have a fast clotting time and yet bleed freely from a slight lesion anywhere, the trouble being probably rather of vascular than of hemic origin.

3. The firmness of the coagulum is an important matter, and can be roughly gauged by this method, although the results cannot be given in figures.

4. Anemia due to hemorrhage is constantly associated with a hastened coagulation time.

5. Acute rheumatism is usually accompanied by a delay in the clotting.

6. The free exhibition of calcium lactate and of citric acid by the mouth in various diseased conditions seems to have no appreciable effect upon the coagulation time of the blood as estimated by this method.

THE PHYSIOLOGY AND PATHOLOGY OF FEVER.[1]

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Of all the symptoms which appear during the various pathological conditions of the human organism, fever, because of its frequency,

[1] Read before the Eastern Medical Society, New York.

occupies the first place. It is quite natural, therefore, that from days immemorial, it attracted the attention of physicians, who tried to explain it and the other disturbances that are connected with it. The subject presents interest not only from its practical point of view, but more so from its theoretical, because it is only after a thorough and clear understanding of the exact causes of fever that proper therapeutic measures may be applied. A great many clinicians and scientists studied these problems from their respective views, and the literature of the subject became burdened with facts. The clinician gathered information from the bed side; he watched the behavior of his patient under the influence of different infectious processes; studied them, and finally learned to recognize them from the character of the symptoms. The scientists attacked the problem from the other side. They produced the disease in animals experimentally by injecting different toxins, or produced one of the many symptoms of fever, and studied their influences on the organism.

In this brief review we will endeavor to present themost important facts and theories that have been accepted in the past few years. The first question that confronts an investigator is: What is the cause of fever?

The Cause of Fever. Clinicians know from experience, that fever is always closely allied to infection, and that its intensity bears a direct relationship to the appearance of a new crop of microorganisms in the blood. The temperature of the malarial patient always rises after sporulation of the plasmodium. Lüdke also found that immediately preceding the rise in temperature, microörganisms are present in the blood of patients suffering with pneumonia and typhoid fever, although their blood was sterile the previous day. These facts at once suggested that the bacteria are responsible for the disturbances.

It was at first thought that the bacteria themselves by virtue of their presence, acted like foreign bodies, and produced irritation of the respiratory, circulatory, and heat regulating centres. In fact, it was demonstrated that the injection of a fine suspension of lycopodium or starch in the blood stream of animals produced a slight rise in temperature. But, it was soon seen that this theory did not work out in all cases We meet with a great many fevers where the infection is only local, and the disturbances are general. We meet with fever in cases of fractures, subcutaneous hemorrhages and resorption of blood, where there is no accompanying infection at all. These facts compelled investigations along entirely different lines.

Billroth[2] and Weber[3] injected the products of decomposed animal and vegetable substances into the blood stream of animals, and obtained the typical symptoms of fever, with circulatory, respiratory

[1] Langenbeck's Arch., 1862, ii, 335.

[2] Berlin. klin. Woch., 1864, p. 39

and nervous disturbances. The injection of substances derived from the protoplasm of non-pathogenic germs produced similar results. Lüdke showed that an animal's own tissues ingrafted into itself, as well as foreign tissues, when absorbed, caused a rise in temperature. It was further shown that the injection of sterilized and filtered bacterial culture was followed by symptoms of intoxication. All these experiments show very clearly and definitely that although the bacteria themselves, by their presence in the tissues, may act as irritants, yet in the production of fever the presence of the toxin, produced by the bacteria, and the presence of substances of albuminous nature (Krehl), produced by the dissolution of the bacterial protoplasm or body cells are of far greater importance. These substances may contain more than one toxin, each having its own specific action. It was shown that the bouillon culture of tetanus bacilli contain in addition to the tetanus producing substances, a toxin which acts on the blood (hemotoxin). From the staphylococci we can isolate a substance leukocydin which has specific toxic influences on the leukocytes. In snake venom, we can isolate a neurotoxin, which acts on the nervous system, a hemolytic substance, hemorrhagin which acts on the endothelium of the bloodvessels, and thrombase which influences the fibrin.

Similar to some of the cells of the animal body, which possess a great many functions and produce a great many ferments, so the cells of bacteria have the power of producing a great many different substances which act injuriously on the human body. Although all have not yet been isolated and the specificity of each has not yet been determined, still it is hoped that they will be in the near future. We must not assume that all bacteria produce the different toxins in the same proportions, nor that all bacteria produce the same toxins. From the fact that the infections with different bacteria produce different reactions on the part of the leukocytes, immunity and formation of antibodies, we may safely conclude that the different species of bacteria contain and produce different toxins.

Regulation of Body Temperature. The normal temperature of the body is maintained at a level, fluctuating between 36.5° to 37.5° C. It reaches its highest point at about 7 P.M., and its lowest point at about 6 A.M. Under normal conditions it seldom passes these limits. The most important factors which are responsible for the diurnal variations in temperature are work, the partaking of meals, and exposure to various stimuli. In fever, the temperature may go up to 41° and 42° C., and in some cases even higher. The factors which influence the normal temperature curve, act in a much more pronounced way in the febrile patient, and the chart presents much greater diurnal fluctuations. The height of the temperature in fever in a great many cases is proportional to the intensity of the intoxication, and may serve as a measure for it. But in the two extremes of life, childhood and old age, it cannot be relied upon. Mild infections in the child

may be accompanied by very high temperature, whereas a most severe infection in the old, may produce a rise of only 1° or 2° C. (Krehl).[4]

The temperature of the normal individual is maintained at a constant level, because of the function of the heat regulating centre, which is situated in the anterior portion of the corpus striatum (Aronsohn und Sachs).[5] This centre stands in close nervous communication with every part of the body, and with all the vital centers in the medulla oblongata, especially the vasomotor centres.

All the vital processes in the cells of the body, be they secretion or motion, are the result of oxidation of organic matter in the cells. The oxidation of these substances is accompanied by generation of heat. This heat is utilized in keeping the body warm. It may be measured in terms of calories. One calory is the equivalent of the amount of heat that is necessary to raise one liter of water 1° C.

The human individual produces when at rest and under normal conditions, 33 calories per kilo. of his body weight every twenty-four hours. In other words, a man of 70 kilos will generate in the course of twenty-four hours, 2310 calories, that is, an amount of heat which will raise 23 liters of water from the freezing to the boiling point. Let this man do some work, and at once the oxidative processes will be increased, and more heat will be generated. All this heat is not retained in the body, but is given off into space. This is accomplished: (1) By radiation and conduction, and (2) by the evaporation of water from the skin and lungs.

It is at once apparent that the amount of heat lost by the body by radiation and conduction depends entirely upon the difference in temperature between the body and the surrounding atmosphere. To prevent the loss of too much heat in the lower animals, nature has supplied them with a coat of fur or feathers, which contain large quantities of stagnant air between. This stagnant air is a very poor conductor of heat. Civilized man resorts to an artificial method of protection against loss of too much heat. He covers his body with clothing, the character of which varies with the climate and the surrounding temperature. At this point we may accept without any reservation, the speculation of MacCallum[6] when he says, ". . . After all, it was this need of artificial heat regulation which probably brought about man's suddenly acquired knowledge of good and evil."

The temperature of the body can be maintained at a constant level only when there is complete calorific equilibrium, that is when the same quantity is eliminated as is produced. Should the heat elimination be greater than the heat production, there at once takes place a lowering of the body temperature. Should, however, the heat production be greater than the heat elimination, the tem-

[4] Das Fieber, Pathologische Physiologie, 1910.
[5] Pflüger's Archiv, p. 37.
[6] Arch. of Internal Medicine, 1909

perature will rise. The function of the heat regulating centre is to prevent these variations.

When a man is exposed to cold, a stimulation of the peripheral nerves takes place. This stimulation results in reflex contraction of the superficial bloodvessels. Less warm blood is brought to the skin, consequently, less heat is lost. Should the exposure continue and the physical process be inadequate for the protection against loss of heat, then a new factor is brought into play—the chemical process. All the muscles are thrown into fibrillary activity, shivering takes place, oxidation is thus increased, and a greater amount of heat is generated, enough to equal the loss. The body temperature remains unaffected.

If, however, the man is exposed to a tropical temperature, little or no heat can be lost by radiation and conduction, because the difference between the body temperature and the temperature of his environment is not great enough. A dilatation of the superficial bloodvessels and profuse perspiration takes place. This perspiration is evaporated, and every gram of water during the process of evaporation takes away 0.59 calories of heat from the body. We see from the experiments performed by Rubner[7] that a man, who was exposed to a temperature of 20° C., evaporated 56 gm. of water per hour. When he was exposed to a temperature of 36° to 37° C., his body temperature being equal to the temperature of the surroundng atmosphere, he could lose no heat by radiation and conduction. The amount of water then evaporated per hour rose to 204 gms. These 204 gms. of water per hour required 120.3 calories, to evaporate. For the twenty-four hours, a total of 2888 calories, the equivalent of the total amount of heat produced by that man. The man's temperature remained constant. This is a good illustration of how perfectly the heat regulating centre acts. It may be stated here, that R. Cohn succeeded in producing dilatation of the bloodvessels and secretion of sweat, by simply raising the temperature of the blood of the carotid arteries on its way to the brain.

The Mechanism of Fever. Having considered the physiology of the temperature regulation, we will take up the subject of the mechanism of fever. It is evident from what was said above, that the rise in temperature in fever can be accomplished only by a disturbance in the balance between heat production and heat loss. There are two possibilities, therefore. Either there is an increase in heat production without a corresponding increase in heat loss, or there is no increase in heat production, but there is diminution in heat loss. In either case a storing of heat in the body will take place. An enormous amount of work has been done on this subject in the past number of years, and the results are very conflicting, undoubtedly due to the differences in the methods employed by the

[1] Die Gesetze des Energieverbrauchs bei die Ernärung, 1902.

different investigators. Time does not allow us to enter in any detailed discussion of these methods and their respective results. I shall only summarize the work which is most complete and very convincing. This work was performed by Likhachev and Avroroff,[8] in Paschutins Laboratory, in St. Petersburg.

They studied the metabolism of a young Russian woman who was afflicted with malaria. She was placed in an oval shaped calorimeter which had a capacity of 2.7 cubic meters. She was made comfortable by being placed on a bed close to the floor. The calorimeter was kept hermetically sealed. Eighty liters of air were driven through the calorimeter per minute, and were made to pass through sulphuric acid for the determination of water, and through potassium hydrate for the determination of carbon dioxide given off by the patient. Before the experiment was begun, the patient was weighed, her food and water for drinking were measured out. After she had been installed and sealed in the calorimeter, ventilation was carried on for one to two hours until an equilibrium in temperature was established. The other twenty-two hours of the twenty-four were divided into eleven two-hour periods. At the end of every hour the patient's temperature was ascertained, also the temperature of the room, air, and of the calorimeter. At the end of every period the weight of the CO_2 and water given off were determined, also the amount of air that passed through the calorimeter and its temperature.

The heat lost by radiation and conduction was determined by noting the changes in the temperature of the calorimeter and the changes in the temperature of the air that passed through it. The heat lost by evaporation of water was measured by determining the quantity of water given off by the patient through her skin and lungs, and by multiplying same by 0.59 calories. The total heat production was obtained from the sum of the values of the heat lost by evaporation of water and by radiation and conduction plus or minus the retention or loss of heat because of changes in the body temperature. This last one was determined from the following formula: $W \times (T \pm t) \times S$. W equals body weight, T equals temperature of body, t equals value of change in temperature, and S equals specific heat of body, which equals 0.83.

The patient was kept in the calorimeter for three days, one normal and two febrile. The results are here tabulated. See table I and Figs. 1 and 2.

The patient was at perfect ease while in the calorimeter. We see from the curve of the normal day, that the heat production fluctuates from 85 calories per hour to 46 calories, and that the total heat elimination throughout the day runs approximately parallel to the former. We also notice that the greatest amount of heat,

[8] Isviesti Imperatorskoy Voenno Medicinskoi Academii, 1902, v, 239. I am indebted to Prof. F. G. Benedict for kindly calling my attention to this work, which was published in 1902, and remained entirely unknown to the western world.

74.6 per cent., is lost through radiation and conduction, and that only 25.4 per cent. is lost by evaporation of water.

On the day of high fever, at midnight the patient was placed in the calorimeter. During the morning, she presented the typical symptoms of malaria. At 1 A.M., the chill set in which lasted for about two hours. The heat production per hour thus rose from 54 calories to 93. The heat elimination, however, sank from 65 calories per hour to 57. This tremendous disturbance in the balance between

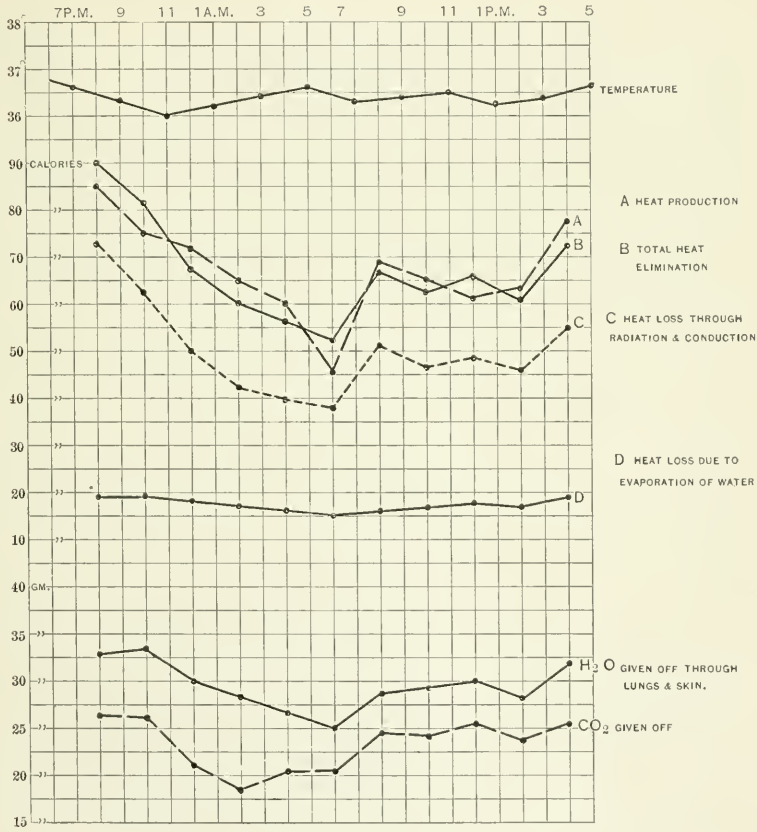

Fig. 1.—Normal day.

heat production and heat loss resulted in heat being stored in the body, and the body temperature rose from 36, to 38, 39, and finally to 39.7° C. These results led the experimentors to conclude that the rise of temperature in fever is due to an increase in the heat production without a corresponding increase in heat elimination.

This increase in heat production is most marked during the period of the initial chill. In long continued fevers, some authors believe there is an increase in heat production only in so far as there is an

increase in the activity of the respiratory muscles and heart beat. Matthes,[9] however, believes that after subtracting the heat produced by the increased activity of the respiratory muscles and increased heart beats, and by subtracting the increased heat produced, due to rise in body temperature, there will still be found an

FIG. 2.— Day of high fever.

increase above the normal. This increase, he believes, is caused by the toxins themselves. As a matter of fact, Krehl and Soetbeer found an increase in heat production in infected cold-blooded animals.

[9] Ueber das Fieber; Die Deutsch. klin. am Eingange des Zwanzigsten Jahrhunderts, 1909, p. 1.

TABLE I.

Condition.	Total heat production. Calories.	Maximum heat production per hour. Calories.	Minimum heat production per hour. Calories.	Heat lost by radiation and conduction. Per cent.	Heat lost by evaporation of H_2O. Per cent.	Food value in calories.	CO_2 given off in grams.	H_2O evaporated from skin and lungs in grams.	O_2 consumed in grams.	R. Q.	Amount of urine. Grams.	N in urine.	C in urine.	Body temperature. (C.)
Normal	1480	91.0	53.0	74.6	25.4	1030	513.0	637.0	406.0	0.92	1796.0	11.4	8.8	36.0 to 36.7
Low fever	1492	78.6	56.6	74.7	25.3	776	520.0	638.0	474.0	0.8	442.0	9.1	7.5	
High fever	1633	112.0	48.0	69.8	30.2	533[1]	587.0	852.0	563.0	0.76	593.0	10.2	6.9	35.8 to 39.7

[1] The food taken on this day is almost one-half of normal. This influences heat production a great deal by eliminating the specific dynamic action of that food.

TABLE II.—Bacilli in 100 Leukocytes.

Temperature.	Typhoid B.	Streptococci.	Staphylococci.	Tubercle B.
36° C.	1080	1400	1210	1110
37 to 37.5	1100	1520	1200	1400
38.5	1120	1560	1590	1580
35.9 to 40	1530	1650	3100	1800
41.5	1040	....	1150	
42.5	610	760		

The cause of the accelerated pulse and respiration during fever can be found partly in the overheating of the body. But we must not exclude the possibility of a specific toxin acting on the cardiac and respiratory centres. The fact that the character of the pulse and its rate are different in different diseases, that it is always slow in typhoid, and very rapid in sepsis, speaks very much in favor of this possibility.

The Effect of High Temperature. It was the belief of the early investigators (Liebermeister, Littern), that the high temperature in fever produced deleterious influences on the organism, and that the fatty and parenchymatous degenerations were due to it. This belief was practically universal, and in the matter of treatment of febrile patients, it was always borne in mind. The works of Naunyn[10] and Unverricht,[11] based upon clinical and experimental observation destroyed these theories. Naunyn showed that animals can be kept for weeks at a febrile temperature without presenting any signs of degeneration. As soon as this was corroborated and the conviction of the harmfulness of the high temperature removed, investigators began to inquire into the purpose of the high temperature in fever. The application of the Darwinian doctrine of the "preservation of the useful" to this case, was energetically opposed by Krehl,[12] who showed that this theory cannot be used in explaining pathological processes.

Rolly and Meltzer,[13] and later Lüdke,[14] studied the influence of the febrile temperature on the different components of the reaction toward infection. Namely, its influence: (1) On the growth of bacteria in the animal body; (2) on the resistance of animals toward bacterial infection; (3) on the bactericytic power of the blood; (4) on phagocytosis; (5) on the bacterial toxins; (6) on the production of antitoxins.

The hyperthermia was brought about by placing the animals in well ventilated, double-walled metal cages, which were kept at a temperature of about 35° to 36° C. by means of a burning flame. This flame was regulated by means of a thermoregulator which was situated between the walls of the cages. The animal's temperature under those conditions rose to about 40° C. The animals that were overheated, after receiving daily subcutaneous injections of one-fourth to one-half the fatal dose of either staphylococci, pneumococci, or bacilli coli communis, lived longer and one-half of them survived, whereas all of the control animals died.

The influence of the febrile temperature on phagocytosis is shown beautifully in Table II.

[10] Arch. f. Experimentelle Pathologie und Pharmacologie, 1884, xviii, 49.
[11] Deutsch. med. Wochenschr., 1883, vol. v.
[12] Lubarsch Ostertags Ergebnisse, 1896.
[13] Deutsch. Arch. f. klin. Med., 1908, xciv, 335.
[14] Ibid., 1909, xcv, 425.

THE TREATMENT OF FEBRILE CONDITIONS.[1]

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It is one of the most hopeful features of modern therapy that it is taking cognizance of the fact that the organism has been perfecting means of defense since first it became the seat of disease and that these means of defense are to be read not merely in the subtile elaboration of antitoxic bodies in the tissues and the marshalling of counter-forces in the blood elements, but also in the alteration of the functions of organs. Emesis as a symptom is primarily an effort to unburden the stomach of deleterious substances; diarrhea is protective in the same sense; cough removes secretions which are both irritants and mechanical impediments to the respiration; pain ensures rest to an affected part and so on. Interference with these symptoms must be undertaken with discretion lest it become pernicious. It is the knowledge of when to let alone and when to interfere that constitutes the art of therapy. Emesis, diarrhea and cough may become a source of exhaustion; pain which has pointed the way to the trouble and hinted the need of rest be illy borne when continued and fever arise to degrees that are incompatible with its purpose and constitute hyperpyrexia. At this point, treatment steps in to modify and assist, not to disregard Nature's signals.

Fever, as the physician knows it, is almost invariably the result of bacterial action, so cannot be dissociated from toxemia; but pyrexia and toxemia show but little parallelism; indeed, the worst forms of toxemia may be accompanied by no pyrexia at all, while a relatively high temperature may be seen with a minimal toxemia. Briefly, then, unless the degree of temperature is inordinately high, that is, constitutes a hyperpyrexia, the treatment of fever is not an antipyretic treatment but an antitoxemic treatment, and such fall of temperature as accompanies our efforts is incidental to them and not the object at which we aimed.

The treatment of fever involves the appreciation of certain broad principles that in the main are physiological. They are not numerous, but they are of fundamental importance. We shall take them up seriatim. (1) rest; (2) diet, including the ingestion of water; (3) fresh air; (4) water locally applied, that is hydrotherapy; (5) drugs; (6) hyperpyrexia. I think it little matters what name we give the febrile process or the organism inducing it. The procedures are much the same.

[1] Read before the Eastern Medical Society, New York City.

Rest. It is a valuable form of mental exercise for a physician to pause occasionally and review some of the fundamental facts of physiology that are relevant to the problem in hand. First one should recall the fact that the sum total of the body's activities are but the expression of the conversion of potential energy of the food stuffs into these different forms of energies; that the body observes an accurate balance between the intake and output; that the law of conservation of energy obtains in the human body as well as elsewhere, and, therefore, when the intake is lessened, the expenditure should be diminished and useless forms of work should be avoided that useful purposes may be subserved.

All this means that in fever rest is imperative and that, as the body cells are expending energy in the elaboration of protective substances and the processes of repair are active in inflamed tissues, muscular unrest and muscular work should be avoided. Physiologists tell us that CO_2, an end product of the combustion of food stuffs in the production of energy may be taken as a measure of the energy of work and heat arising in the body and that the same man who during sleep eliminates 22 grams of CO_2 an hour will, when awake and exercising the greatest amount of muscular relaxation possible, eliminate 31 grams, and under conditions that we ordinarily term rest, such as most patients observe eliminates 38 grams. These figures are cited to call attention to what a relative term "rest" is.

Again, in fever, the vascular and other vital centres are all too often sought out and when we recall the lessened number of heart beats in recumbency and slight fall of pressure under the same circumstances we appreciate the economy exerted in behalf of these organs by rest.

Rest means something more than going to bed, though that is imperative. It means that the bed must be comfortable, so that energy shall not be wasted in the effort to maintain strained positions or avoid uncomfortable ones; it means competent nursing; it means measures directed at sleeplessness and at delirium. Mental rest is equally important, for though the loss of energy in the mental processes *per se* is minute, strained and restless muscles are the results of anxiety and concern, as, indeed, are perverted functions in many organs. Leave the sick room to the sick; exclude solicitous friends. Job's comforters, mourners before the fact. Avoid the introduction of business matters or domestic concerns, and let quiet and order reign. The contrast between a well-ordered, neat, cool, sick-room, and a hot stuffy room with six to ten visitors, gas-jets in full action and Babel and Chaos regnant is one of the most striking that can be witnessed.

Diet. Again let us appeal to physiology for facts. They are (1) That the amount of work done and the amount of heat given off by the human body each day is derived from the food taken in that

day or stored in the body from previous meals and that that store is not inexhaustible. (2) That the amount of energy supplied a man at rest each day amounts on the average to 33 calories[2] per kilo of body weight which in a man of average weight amounts to 2300 calories. (3) That a sick man at rest requires as many calories of energy as a well man. (4) That fever makes certain demands in excess of those obtaining in health, because the increased temperature *per se*, that is, pyrexia above 102° F. increases the output some 25 per cent. on an average, thus raising our caloric requirements to 40 per kilo or 3000 for the man of average weight. (5) That the toxins of disease are destructive of body tissue in varying degrees, a destruction which may be overcome or minimized by a sufficient intake of food. (6) That the amount of proteid needed each day in health is about 100 grams. (7) That in fever the requirement is about the same or may be a trifle less, 75 to 85 grams, which is enough to prevent proteid loss when enough carbohydrates are added. The appreciation of these facts is increasingly important in the prolonged fevers, such as typhoid, certain bronchopneumonias or septic conditions.

One other fact is of special importance in orientating us correctly with reference to this subject; namely, that such studies as have been undertaken to determine the efficiency of the processes of digestion and assimilation of the foodstuffs in fever show that except at the onset these processes are scarcely impaired.

A sufficiency of food is an important item in the treatment of fever, because, as has been intimated already, an insufficiency leads to destruction of the body substance with the production of toxic material in the process, an autointoxication.

Briefly, in the beginning of fever, do not push the food; respect the meaning of anorexia; but later increase daily to the approximation of theoretical needs. Remember that there are other foods than milk that are easily digested, including cereals, bread, butter, eggs.

Water is an important item in the treatment of fever; all the water that the patient wants and his wants should be determined by offering him water at frequent intervals, as his cerebral condition may be such as to prevent his asking for the amount he needs.

Studies of the water intake in certain infections such as pneumonia show that the amounts are sometimes extraordinary, 3000 to 5000 c.c. a day, and that the patients who are given a sufficiency seem to do best.

Fresh Air. That the sick require fresh air would seem a thesis too simple to require emphasis, and yet many physicians make no protest against the vitiation of the sick room by a swarm of visitors and burning gas-jets and make only a half-hearted appeal for an open window.

[2] A calory is that amount of heat that will raise one kilo of water through 1° C.

The bad effects of ill ventilation are due largely to the accumulation of CO_2 gas. In the country pure air contains about 3 volumes of the gas to 10,000 volumes of air. In rooms and work-shops it may rise to over 30 volumes, and in the night with the gas burning to nearly 50.

We consider it niggardly in the hospital if we do not allow 1000 cubic feet to each sick infant, but how many of our patients get 1000 cubic feet of fresh air to themselves in the sick room.

The increase of CO_2 is not the only evil in ill ventilation, for contamination of the air with bacteria and varied forms of dirt must ensue; while, heat, moisture, and odors add their depressing effects.

But there is another quality to fresh air when taken in the open that adds materially to its value; it is the element of cold given either by the temperature of the air or by the effects of its movement. Pembrey, in a masterly article on Respiratory Exchange in Hill's *Recent Advances in Physiology and Biochemistry*, says "The success of the open-air treatment depends it would seem, not so much upon any greater purity of the air as upon free exposure; the open air increases the combustion and respiratory exchange improves the appetite and augments the metabolism."

More than that, it is an every-day demonstration to the students in our ward that the exposure of the febrile patient to the open air will induce a rise of blood pressure over that obtained in a well-ventilated ward equal to or better than that obtained from our usual vasomotor stimulants, with the added advantage of being continuously sustained which does not obtain with the drugs.

I am convinced of the very great value of the open air treatment of fever. The pulse and respiration improves, the cerebral intoxication diminishes and the patients are almost universal in their commendation of it.

To reap success, however, the technique must be correct. The patient's bed must be so made as to keep the body always warm, by enclosing the bed in impermeable material like rubber sheeting or paper, the use of the hot water bottle, and by sheltering from winds. The good effects, I believe, come from the action of cold on the nerves of the mucous membrane of the nose or of the face, producing reflexly an improved vascular condition.

Water Locally Applied, Hydrotherapy. I am firmly convinced of the efficacy of remedial measures, operating on the various functions through the surface of the body, that branch of the healing art included under the head of physical therapy. This field has been grossly neglected for various reasons; in part because of the dominant position occupied by drug administration in the minds of most practitioners and very largely because of the time and effort entailed in the administration of these measures and the acquisition of a proper technique.

Water is a very valuable instrument in combating the evil results of fever. Baruch, whose persistent advocacy of hydrotherapy constitutes a real service to American Medicine and has not received half the recognition it deserves, points out that the value of water lies not so much in its physical constitution as in the fact that it is an admirable material for the conveyance of heat and cold and that strickly speaking, thermotherapy is a better term than hydrotherapy in the use of water. A few facts should be borne in mind in considering hydrotherapy. (1) That we are aiming rather at the toxemia than at the pyrexia. (2) That the reaction to the use of cold water is the *sine qua non* of success. (3) That friction is as important as the cold in many of the procedures.

The good effects of the cold water are obtained largely through the nervous system. The impulses pouring in through the countless nerves upon the centres result in a slower, stronger heart beat, and an improved vasomotor tone, which can be measured in terms of an increased blood pressure; respiration is deepened, cerebral processes improved, and metabolism enhanced.

Without detailing the various procedures, one may mention as the best known, the Brand bath in typhoid fever and the chest-compress in pneumonia.

Through the cold air and cold water we effect much the same results; the time of year, the facilities of the environment and the reaction of the patients determine an indication for one or the other.

Drugs. Drug administration, like the other measures, is aimed not at the pyrexia but at the toxemia, and that the fever is influenced is due to a relief of the toxemia or the conditions determined by it.

Cathartics occupy an important position among the drugs, because they prevent a stagnation within the bowel and the consequent absorption of putrefactive products.

The toxins of disease impinge upon the vital nervous centres and upon none more certainly than upon the vasomotor centre. Our great dread in the severe intoxication, such as typhoid fever, pneumonia, diphtheria, scarlet fever, and sepsis is a circulatory failure. The term "circulatory" is used advisedly, because upon this we can all agree, but when we try to fix this failure in the heart or in the vasomotor apparatus an abundant opportunity for difference of opinion arises.

My own belief is that the careful studies of this question show that in the large majority of cases it is the vasomotor mechanism that is at fault. For this reason my preference is for drugs that act either on the vasomotor centre or on the vessels. My own choice at the present time is for caffeine and I think it should be given in sufficient dosage and so administered as to guarantee its arrival at the goal desired. I give it in the form of one of the soluble double

salts, that of caffeine and sodium benzoate or caffeine and sodium salicylate, in doses of five grains every four hours, and such studies as I have made upon its effects on blood pressure show that its effects do not last even throughout this period. Next to caffeine, I use a 10 per cent. or 20 per cent. solution of camphor in olive oil and use more than the usual dose, giving at least five grains every four hours, hypodermically, often alternating with the caffeine, thus giving a dose every two hours. Personally I have less faith in strychnine.

That we can exclude the heart in all cases I do not believe and so, if the vasomotor stimulants are not efficacious, one uses digitalis in doses of one-half an ounce of the infusion three or four times a day and appreciating that it will not become operative in less than twenty-four hours, may use as an initial dose one-half milligram of strophanthin intramuscularly.

No mention has been made so far of the antipyretics. In the early stage with bounding pulse, aconite may afford some relief by slowing the heart through the vagus, the coal tars may be used with relief of headache and other pains, but here again the fall of temperature is incidental. These drugs are depressants and should never be used where the circulation is impaired.

Hyperpyrexia. As has been said, fever may be looked upon as of purposeful intent, as a conservative effort on the part of the organism to accomplish something useful to itself. If this be so, measures directed at the fever as such are misdirected if not pernicious, and it will be noted that the treatment of fever outlined in this paper has been directed at the toxemia accompanying the febrile movement rather than at the latter; but as was said in the beginning, any symptoms primarily useful may in the end become harmful; one may say that Nature has overshot the mark. Excessive temperatures fall into this category as well as prolonged sustained temperatures.

Hyperpyrexia threatens cell function and cell integrity as increased proteid destruction shows. We see its effects best in insolation and in certain rheumatic fevers. In these cases reduction of heat is life saving.

We have no better method than the direct application of cold in the shape of cold baths or ice rubbed upon the surface of the body. The patient may be put into a bath of 90° F. and the water cooled down to 70° F. to 75° F. The body is kept immersed until the body temperature falls below the danger point, but it is wise to remove the patient when it falls to 102° F., as collapse may ensue on efforts to reduce it to normal. If such occurs, stimulants and heat are indicated, as in collapse from any other cause.

Antipyretics of the coal-tar group are not comparable in efficienye or safety to cold water, but may be used where it is impossible to use the latter.

No attempt has been made in this paper to go into details; only generalizations have been laid down with special emphasis given to those branches of therapy commonly neglected, and for this reason serum therapy, which is specific for individual disease has been omitted.

CYSTS OF THE SPLEEN.

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The following case occurred in the Pennsylvania Hospital, upon the service of Dr. John H. Gibbon, during my term of service there, and on account of the rareness of the condition, is though of sufficient interest to report.

The patient, B. G., a female, aged twenty-five years, first noticed seven years ago, a slight swelling in the left side of abdomen and under the ribs in the splenic area. Since then this mass has gradually enlarged down, into, and across the abdomen. During the last year the growth was much more rapid, so that the tumor reached across the abdomen to a line drawn upward from the right iliac spine. Patient did not remember ever having been hit or struck in the region of the spleen. She complained of soreness over the mass, with at times slight nausea, but no vomiting, which was attributed to the mass. Her general health remained about the same as previous to the discovery of the tumor, but in the last year on account of the more rapid increase in growth, she though she had grown weaker. Her appetite was good, bowels constipated. She menstruated first at thirteen. Since then it has always occurred regularly with some pain the first day.

Her past medical history, family, and social history had no bearing upon the present condition.

The physical examination showed the patient to be a rather thin, somewhat anemic looking young Irish woman. Her complexion was pasty. Her teeth were in splendid condition. The lungs were normal. The cardiac dulness extended from the first interspace above, to the right border of the sternum on the right, and on the left, to the fourth rib directly below the nipple. The sounds were regular and with a good muscle tone, except that at the apex a soft mitral systolic murmur was heard. The abdomen showed the presence of a large tumor. This was largest and most prominent in the epigastrium. It was hard and in the upper part there was a distinct wave of fluctuation. This tumor extended above from the beginning of cardiac dulness, down the midaxillary line to within two inches of the anterior superior spine, then out one and one-

half inches to right of the umbilicus and then up to just within the liver dulness. The mass was movable on respiration and seemed to be the spleen or a cyst of the spleen. The left border was sharp and distinct, the right was dull and hard to determine. The liver dulness extended from the fifth to the eighth rib. The organ was not palpable. There was no change in the lymphatic system except that a few glands, small and discrete, could be felt in the cervical and the inguinal regions. Knee-jerks were not elicited.

The blood count was as follows: Red blood cells, 4,360,000; hemoglobin, 70 per cent.; leukocytes, 9400. The differential count showed polymorphonuclears, 65 per cent.; lymphocytes, 29 per cent.; mononuclears, 2 per cent.; transitionals, 1 per cent.; eosinophiles, 3 per cent.

On admission, the urine had a specific gravity of 1030. It contained a slight trace of albumin, but no casts, pus, nor sugar. Immediately before operation, the urine contained no albumin and was normal in every respect.

The operation was performed on September 14. Morphine, atropin, ethyl chloride, and ether were the anesthetics employed. An incision was made over the left upper rectus, the fibers of which were split. Upon opening the abdomen, a large cyst was found adherent to the diaphragm and surrounded, except in the upper part, by splenic tissue. This was freed from all surrounding adhesions and then tapped. Clear yellow fluid was removed, 100 ounces in amount. The splenic vessels were then tied off and the whole huge cyst and spleen amputated. With a great deal of difficulty about a half dozen bleeding places in the adhesions were tied off and all hemorrhage completely stopped. The peritoneum was closed with continuous catgut. The fasciæ were similarly closed, and a subcutaneous stitch put in, the edges of the wound being accurately approximated with sterile strips of zinc oxide adhesive.

The patient reacted fairly well. She had very slight postoperative nausea and no vomiting. Immediately after operation, her urine had a specific gravity of 1035. There was also a faint trace of albumin, but no casts nor blood.

The day after operation, the patient had considerable pain, particularly along the course of the diaphragm. This seemed much relieved by a broad adhesive strip along the diaphragm borders. Two days later her condition was good, though she had considerable abdominal distention. Two days later her condition continued good. She still had a little elevation of temperature, accounted for by several small abscesses under the adhesive strips. Eight days later she was improving rapidly, the skin wound was clean and completely healed. The patient had absolutely no subjective complaints, though she still had slight fever at times. Her blood count was as follows: Red blood corpuscles, 4,642,000; hemoglobin, 90 per cent.; leukocytes, 11,400; polymorphonuclears, 70.6 per

cent.; lymphocytes, 14.6 per cent.; mononuclears, 10.2 per cent.; eosinophiles, 2.4 per cent.; transitionals, 2 per cent.; basophiles, 0.2 per cent.

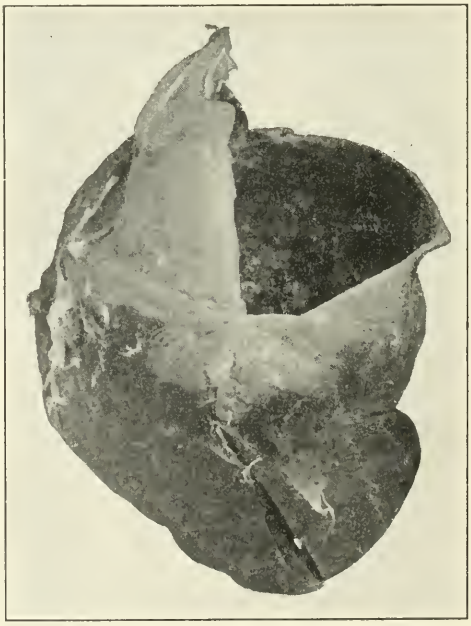
Two weeks after the operation patient was up and walking around. Her condition was very good. Her third blood count, eighteen days after operation, showed: Red blood corpuscles, 3,916,000, hemoglobin, 78 per cent.; leukocytes, 13,900; polymorphonuclears, 60 per cent.; lymphocytes, 24 per cent.; mononuclears, 11 per cent.; transitionals, 5 per cent. A little less than a month after operation she was discharged cured.

The condition of the patient at the present time, nine months after operation, is excellent. She has gained in weight, and in every way her general condition is good. Physical examination shows a scar well healed; no pain or tenderness anywhere in the abdomen; nor can any abnormalities be palpated. No enlargement of the superficial lymph glands is found beyond a few small discrete glands noted before operation. This, however, is to be expected, as such an enlargement would probably take place only in the hemolymph glands.

The recent blood count is as follows: Red blood corpuscles, 4,400,000; hemoglobin, 80 per cent.; leukocytes, 17,700; The differential count of 200 cells shows: Polymorphonuclears, 70 per cent.; lymphocytes, 25 per cent.; mononuclears, 3 per cent.; transitionals, 1 per cent.; eosinophiles, 0.5 per cent.; undetermined, 0.5 per cent.

Pathological Descriptions. The specimen consists of a spleen at the upper margin of which a huge cyst has been opened and collapsed. The entire specimen weighs 400 grams. It is more or less rounded and measures about 18 cm. across. The cyst occupies the upper posterior region of the spleen, so that the spleen forms a semicircular wide rim, 6 to 8 cm. across the lower and anterior margin of the cyst, and is surrounded on three sides by spleen tissue. Excluding the cysts, the spleen itself is much enlarged. The surface of the cyst is fairly smooth, but is covered here and there with fibrous tags (see figure). The spleen is dull purplish red in color, and is of medium consistency. The cyst contained at operation a large amount of yellowish-brown fairly thin fluid, containing a considerable amount of cholesterin crystals. The covering of the cyst is white and opaque. When opened it is found to be a single cavity, almost the size of a football. On the inner surface, however, it is quite smooth, reddish in color and shows in many places yellowish masses which look like cholesterin crystals. The wall measures about 5 mm. in thickness. The spleen on section shows a smooth reddish-gray surface. The Malpighian bodies are visible. The trabeculæ are not prominent. The cyst wall comes in such close approximation to the spleen that it appears to be an integral part of the organ.

Microscopic Examination. Sections through the spleen pulp. The pulp contains very little blood. The venous sinuses are all well defined, and there seems in places to be some increase in the connective tissue of their wall. The tissue appears very cellular, and many of the venous sinuses contain a few polymorphonuclear leukocytes and small round cells. The malpighian bodies are large. The germinal centres are swollen. About the periphery one occasionally sees uninuclear giant cells of epithelioid type. The trabeculæ are not especially prominent. The wall of the cyst is formed of dense connective tissue containing few cells and appearing in places almost hyaline. There is little cellular infiltration but here



Spleen containing cyst that has been opened.

and there a few small bloodvessels are seen between the connective tissue fibers. Occasionally a few isolated plasma cells, epithelioid cells, or small round cells are seen between the strands of dense connective tissue. In one section free blood is also seen between the fibers. The wall of the cyst is not lined by cells.

Anatomical Diagnosis. A cyst with dense connective tissue wall, either arising about the capsule of the spleen or in the spleen itself.

Examination of the Cystic Fluid. Specimen consists of 75 c.c. clear straw-colored fluid, in which are fine, transparent, yellowish particles. Reaction, alkaline; specific gravity, 1030; albumin, 13 per cent. Microscopically many cholesterin crystals are found. Inoculation of various culture media proved negative.

Cysts of the spleen may be classified as follows: (1) Dermoid; (2) echinococcus or parasitic; (3) non-parasitic, (*a*) unilocular, serous, hemorrhagic, lymphatic; (*b*) multilocular.

Of the first variety of cysts, but one has ever been described, the classic case of Andreal,[1] reported in 1829.

The second variety is rare but commoner than the other varieties, and is most frequently found in those countries subject to hydatid disease. In proportion to the number of hydatid cysts occurring in other parts of the body, the incidence of hydatid of the spleen, according to different authorities,[2] is from 2 per cent. to $3\frac{1}{2}$ per cent. of all cases. These, for the most part, have been treated by incision and drainage, but numerous cases have been treated by splenectomy. Johnson,[3] in 1908, collected 23 cases thus treated, with 4 deaths. Since then none has been reported, although Gill[4] reports a case with postmortem, occurring in England, of a Portuguese laborer, who died as a result of a huge hydatid cyst of the spleen.

The third variety, non-parasitic cysts, both clinically and when accidentally found at the autopsy table are very rare. Powers,[5] in 1906, found 32 cases of non-parasitic cyst reported in the literature. Johnson,[6] writing two years later, added 6 more cases, while Bircher[7] finds 33 cases of cyst treated surgically. Since then 4 other cases have been described. The case Bircher reports, he treated by resection with fatal termination. He also quotes the case of Hedinger in which splenectomy was done. Huntingdon[8] reports the third case, and Fowler,[9] the fourth, although the latter's case was not a typical serous cyst, but consisted of a spleen riddled with small cysts, in which the diagnosis of lymphangioma was made.

At autopsy, Henrieius[10] says, the condition is rarely found, and mentions 6 cases in the literature of serous and non-parasitic cysts. Concerning the pathogenesis of serous cysts of the spleen, several theories have been advanced.

1. Many serous cysts have unquestionably arisen from hematoma. This may be due either to a rupture of a normal splenic vessel, most frequently subcapsular from trauma, or to the rupture spontaneous or traumatic, of a diseased bloodvessel, with extravasation of blood into the splenic pulp and later encapsulation. The solid constituents of the blood are, says Moynihan,[11] deposited in

[1] Grundriss der path. Anat., 1830, p. 257.

[2] Thomas, Allbutt's System of Medicine, iv, 456; Litten, Diseases of the Spleen, Nothnagel's Encyclopedia.

[3] Annals of Surgery, 1908, xlviii, 50.

[4] British Med. Journal, 1910, i, 1545.

[5] Annals of Surgery, 1906, xliii, 48.

[6] Loc. cit.

[7] Deut Ztsch f Chir., 1908, xcii, 323.

[8] Trans. Amer. Surg. Assoc., 1907, xxv, 336.

[9] Surg., Gynecol., and Obstet., 1910 xi, 133.

[10] Arch. f. klin, Chir., 1904, lxii, 138.

[11] Quoted by Johnson, loc. cit.

lamina upon the walls of the cyst, the fluid contents thereby becoming clearer.

2. Non-parasitic cysts of the spleen may arise from changes in lymphangioma, as in the case of Fowler.

3. The theory has been advanced by Ranggli,[12] that cysts of the spleen arise from infoliation of the peritoneal endothelium, subsequently stimulated to growth and cyst formation.

4. Beneke[13] believes cysts of the spleen may arise from rupture of the capsule with protrusion of the splenic pulp, the latter proliferating and subsequently becoming cystic.

5. Litten,[14] quoting Böttcher, thinks there is a softening of the pulp with necrosis following occlusion of vessels due to amyloid degeneration.

Mueller,[15] in a recent paper, has gone extensively into the subject of pathogenesis of small cysts of the spleen, and has found them in 11 per cent. of his series of autopsies. Of the large unilocular cysts, he says, without further study and from the lack of experimental work, no definite causative factor can be given.

The present case, although giving no history of trauma, is probably hemorrhagic in origin. The walls of the cyst are more or less laminated, and old blood pigment is found in the cyst wall. The contents were albuminous and of a high specific gravity.

Pathology. The contents of the unilocular cysts may be either serous, hemorrhagic, or chylous. In the first type the fluid is clear, yellowish in color with a low specific gravity, as a rule from 1005 to 1010; albumin may or may not be present, while cholesterin crystals are invariably found. In the second type blood is found, the fluid is turbid, the color varies from a yellow red to a dark brown red, while albumin is always present. Microscopically red blood cells and cholesterin crystals are always seen. In the third type, lymphatic cysts, the specific gravity is much higher, the fluid is turbid and grayish white in color. Microscopically red blood cells, lymphocytes, and cholesterin crystals are found.

Unilocular cysts may vary much in size and have been reported up to the size of a football. All those found at operation have been large. They are surrounded by chronic inflammatory tissue and attached more or less firmly to the surrounding tissues by adhesions. The wall of the cyst is dark in color and varies from 2 to 5 mm. in thickness. The splenic parenchyma may be entirely destroyed or only that of the pole from which the cyst arises, usually the lower pole. The inside of the cyst wall is, as a rule, laminated and divided by thick ridges, and in its fresh state is smooth and glistening. Microscopically the walls are found to consist of dense con-

[12] Inaug. Diss. Zurich., 1894.
[13] XIII Internat. Kongres für Medizin, Paris, 1900, p. 317.
[14] Loc. cit.
[15] Arbeiten a. d. Geb. d. path. Anat. u. Bakter., Tübingen, 1910.

nective tissue, lined with endothelium, and containing blood pigment.

It is the opinion of Monnier,[16] that the majority of non-parasitic cysts occur in women, usually during the menstrual cycle. The large number in menstruating patients is due to hyperemia and consequent relaxation of the period. In the reported cases, the age of the patients varies, but no cysts have been reported in individuals under seven years of age, and only three under fifteen years.

The fact that so few patients were under fifteen years of age would seem to make developmental fault a rare factor in the causation of the condition, while on the other hand, the history of trauma in so many cases shows conclusively that there has been at some time an injury to a splenic bloodvessel.

Symptomatology. In most cases the symptoms are those of a slowly growing tumor in the left hypochondrium. As the tumor increases in size, pressure symptoms, or symptoms due to the mechanical weight of the mass, may develop. These are evidenced by digestive disturbances, flatulence, at times nausea and vomiting as the result of pressure on the stomach, and constipation, from pressure on the bowel. This is well illustrated in my case, as practically the only subjective symptoms were nausea and constipation. A sense of soreness may also be noticed over the mass, while pain, from mechanical traction, referred toward the left axilla and shoulder, is also frequently present. Added to this is always a sense of discomfort. This was also noticed in the present case, and was to be expected, considering the size of the mass, which extended down and well over to the right of the umbilicus and filled completely the epigastrium and left hypochondrium. Objective symptoms are those of any large mass. The site of occurrence, the fact that the tumor dulness is confluent with the splenic dulness, the direct connection frequently found with the spleen by palpation, and the moving of the mass with respiration, all point to the spleen as the site of the origin of the tumor. The cystic character of the tumor is readily recognized by the waves of fluctuation, easily elicited.

In the blood before operation no marked changes have been observed, but the postoperative changes in the blood from splenectomy have been many and varied. In those cases reported with full blood counts there has always been noted a decrease in the hemoglobin and red blood cells with leukocytosis. Some observers have found lymphocytosis, others an eosinophilia, others, the presence of many large mononuclears with a gradual return to the normal differential count in a period of from three to six months. In the present case, shortly after the operation, a considerable increase in the relative number of large lymphocytes occurred,

[16] Beiträge zur. klin. Chir., 1903–04, xli, 181.

but the examination recently made does not show this, although there is still a persistent leukocytosis.

Treatment. In regard to operative procedures in cysts of the spleen a variety of means has been used in the past, as injection with iodine, drainage, and so on. Apparently only three methods are now employed: (1) Resection of cyst, (2) drainage or drainage with marsupialization, and (3) splenectomy.

Bircher finds 4 cases treated by resection of the cyst, with 1 death, due to postoperative ileus. Two others are reported by Powers, making a total of 6 treated by this method. Of the second method, 8 cases have been reported, with one death.

Splenectomy for serous cysts of the spleen has been performed, according to Johnson, nineteen times up to 1908. An additional case has been found by Bircher, the case of Hedinger. Fowler's case was also treated by splenectomy, although not a serous cyst. The case I have just described, operated upon by Dr. Gibbon, brings the list up to 21 with no fatalities.

In conclusion, I wish to express my thanks to Dr. Gibbon for permission to report the case and Dr. Longscope for the pathological description.

A CASE OF LATE HODGKIN'S DISEASE (LYMPHOMA GRANULOMATOSUM), WITH REMARKS ON VARIOUS CASES PRESENTING THE CLINICAL PICTURE OF SPLENIC ANEMIA (BANTI'S DISEASE).[1]

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The patient, H. A., aged twenty-seven years, a German hairdresser in London, was admitted to the German Hospital, on September 29, 1910. Though I saw him once, myself, in February, 1909, I am chiefly indebted for the previous history of the case to Dr. P. P. Daser, under whose care the patient had been before admission to the German Hospital. There was a doubtful history of syphilis about 1905, but the present illness apparently commenced in November, 1908, with a swelling of the right side of the neck, which increased fairly rapidly in size, though it caused no pain. On February 1, 1909, the patient appeared slightly anemic, but fairly well-nourished, weighing 120 pounds. On the right side of his neck was a movable tumor about the size of an apple, situated beneath the middle third of the sternomastoid muscle and apparently formed by a mass of discrete, enlarged, lymphatic glands.

[1] Read before the Medical Society of London, April 10, 1911.

Smaller nodules could be felt lower down in the neck on the same side and some also on the left side. No enlargement of the lymphatic glands elsewhere was detected. A blood film (February 16, 1909) showed slight leukocytosis.

The patient was treated by intramuscular injections of an arsenical preparation, soamin, about every third or fourth day, and at first he seemed to improve. On March 12, 1909, the glandular protrusion on the right side of his neck was scarcely noticeable by sight, though the glands could still be felt. Then he suffered from fever, vomiting, and general malaise (no diarrhea), and kept to his bed for a time. A doctor who attended him thought he had influenza. On April 3, 1909, he looked paler and thinner, weighing only 108 pounds, and the lymphatic glands again had increased in size. Moderate enlargement of the axillary and inguinal lymphatic glands could likewise be detected. There was no ascites and neither the spleen nor the liver could be felt. Iron and a simple tonic medicine were prescribed. He gained in weight and apparently felt better, but after April he did not come under observation again for a considerable time. He was apparently not taking arsenic. In December, 1909, he wrote that he had a febrile attack, similar to that of March, 1909. This weakened him, but was accompanied or followed by the almost complete disappearance of the swelling on the right side of his neck. Two weeks afterward, however, the lymphatic glands began again to increase in size. When seen on September 26, 1910, he said that for the last five weeks he had been ailing, with loss of appetite, fever, and emaciation. He looked thin and pale; his temperature was 104.6° F., and his pulse 120 to the minute. The lymphatic glands could be felt enlarged, but were smaller and harder than when he was first seen, in February, 1909. The liver and spleen were both enlarged, especially the latter, which was hard and slightly tender to palpation. The urine was free from albumin and sugar. Blood films showed distinct leukopenia.

He was admitted to the German Hospital on September 29, 1910, and there his pyrexia and cachexia continued. The fever was of an irregular septic type, the temperature generally varying between 100° and 103° F. The pulse was frequent and weak. Ascites and jaundice developed in the second half of October, and the jaundice gradually increased in intensity. The feces were pale and the urine contained bilirubin, as in cases of obstructive jaundice.

On November 15, 1910, I noted that he was very feeble, jaundiced, and emaciated, with smooth and uniform enlargement of the spleen and liver. The spleen reached downward to just below the umbilical level. The hepatic dulness commenced above at the sixth rib in the right nipple line, and the lower edge of the liver could be felt at about the umbilical level. The heart and lungs showed nothing special. The tongue and mouth were very dry.

The lymphatic glands in the neck could be felt slightly enlarged, but the axillary glands could not be felt at all, and those in the groins were hardly larger than they are in many normal individuals.

Death occurred in a condition of collapse on November 23, 1910. The fever had continued up to the middle of November, but during the last days of life the temperature was usually subnormal and there was a good deal of diarrhea. The urine, when tested about that time, contained 1 per mille albumin. There was little ascites, but a good deal of edema. A few purpuric marks were seen on the abdomen, in lines, as if he had scratched himself, but the jaundice was never accompanied by definite pruritus.

In the hospital, von Pirquet's cutaneous reaction for tuberculosis had given a negative result; so had Widal's reaction. Wassermann's seroreaction for syphilis, performed by Dr. H. R. Dean, at the Lister Institute, was likewise found negative.

A blood examination by Dr. G. Dorner, on September 30, 1910, gave: Hemoglobin, 56 per cent.; red cells, 3,333,330 in the cubic millimeter; color index, 0.86; white cells only, 2480 in the cubic millimeter; no eosinophilia. A differential count of 500 white cells (October 25, 1910) gave: Polymorphonuclear leukocytes, 84 per cent.; small lymphocytes, 3 per cent.; large lymphocytes, 1.7 per cent.; large mononuclears, 7 per cent.; transitionals, 4.3 per cent. Only one nucleated red cell was seen during the count of 500 white cells. The red cells showed anisocytosis and moderate poikilocytosis, as in secondary anemias. On November 12 the hemoglobin was only 35 per cent.; red cells, 1,910,000 in the cubic millimeter; color index, 0.9; white cells, 4124 in the cubic millimeter.

Necropsy and Microscopic Examination. Body much emaciated and jaundiced. The brain and cerebrospinal fluid are not bile stained. The brain weighs 42 ounces and shows slight apparent atrophy of the convolutions. The pericardium contains about 70 c.c. of clear bile-stained serous fluid. On the heart (weight, 9 ounces) are a few pericarditic patches; there is some old thickening of the mitral valve. No atherosclerosis of the aorta or coronary arteries noted. There is chronic indurative pneumonia (as proved by subsequent microscopic examination) of part of the middle and upper lobes of the right lung. Both lungs show hypostatic edema. Pleuritic adhesions are present on both sides. No pulmonary tuberculosis. The peritoneum contains 2400 c.c. of somewhat turbid, bile-stained, ascitic fluid, which is found by microscopic examination to owe its turbidity to the presence of fairly numerous white corpuscles. No evidence of tuberculous peritonitis.

Spleen. Weight, 32 ounces. Uniformly enlarged; rather hard; surface smooth, but showing patches of perisplenitic thickening of the capsule; also one or two scars, which on section are found to be connected with small anemic infarcts. The splenic substance is of a red color and contains numerous small miliary to pea-sized, pale nodules, and a few small hemorrhages.

Liver. Weight, 66 ounces. The surface is smooth and even, with the exception of a little old patchy perihepatitis; it is of greenish color with scattered spots of red. On section, the hepatic substance is found to contain a few pea-sized pale nodules. The red spots beneath the capsule are evidently due to the presence of similar minute nodules, into which hemorrhage has taken place. The common bile duct during life was probably obstructed by a large, chestnut-sized lymphatic gland in the hilum of the liver, but at the necropsy, by firm pressure on the gall-bladder, some bile can be squeezed out through the ducts into the duodenum.

In the kidneys, which weighed together 12 ounces, a little patchy greenish coloration observed in the cortex has been found by subsequent microscopic examination to be probably due to the presence of bile-stained casts in the renal tubules. Nothing special noted in the suprarenal glands, pancreas, stomach, intestines, thyroid gland (rather large), prostate, testes, urinary bladder, abdominal aorta, or great abdominal veins.

The lymphatic glands are widely affected in the thorax and abdomen. Some of the bronchial glands, which are pigmented, are of about the size of large cherries, and the glands in the posterior mediastinum, close to the spinal column, are likewise enlarged. The mesenteric glands vary from the size of a pea to that of a chestnut, some near the spleen and at the hilum of the liver being specially noticeable. One, as large as a chestnut, in the hilum of the liver is hard, colorless, and almost translucent on section. Several of the lymphatic glands in the neck are as large as a hazel-nut. No matting together of lymphatic glands, as in tuberculosis, observed anywhere.

The bone marrow examined in the shaft of the left humerus is red, with small white nodules in it.

I am greatly indebted to Dr. J. C. G. Ledingham for the following report of the microscopic appearances: A lymphatic gland. The fibrosis of the reticular structure of the gland characteristic of the later stages of Hodgkin's disease (lymphoma granulomatosum) is so far advanced that only small patches of lymphoid tissue remain. Some of these, however, present the typical epithelioid cells and giant cells found in Hodgkin lesions. The giant cells have, as a rule, vesicular nuclei, but in some cases the nuclear chromatin is markedly pyknotic. In the interstices of the fibrotic areas plasma cells are exceedingly numerous, but the great majority show lobing and karyorrhexis of their nuclei. Some giant forms of plasma cells are also present. No necrotic areas are seen on section. Other lymphatic glands examined are characterized mainly by fibrotic changes, typical lymphomata with giant cells being absent. Eosinophilic foci are not found. Many of the perivascular lymph spaces contain large numbers of streptococci. They do not appear in the lumina of the bloodvessels.

Spleen. The structure of the spleen is essentially similar to that of the lymph gland, except that the fibrosis is still further advanced and necrotic areas are present. Normal lymphoid nodes (Malpighian corpuscles) are very scarce, but here and there a typical lymphoma is found with epithelioid and giant cells. The necrotic areas are surrounded by numerous effused blood corpuscles and cells containing hemosiderin are very frequent. Small calcified areas staining well with hematoxylin occur in some of the vessel walls and in the necrotic portions. The sinuses contain large numbers of desquamated endothelial cells.

Liver. The liver nodules resemble the spleen in structure. They have evidently been derived from lymphoid structures in the portal areas. Fibrosis is well advanced, but occasional lymphomatous nodes are left, containing scanty giant cells. The bile ducts seen in the fibrotic areas show well-marked proliferation of their epithelium, Dr. Ledingham had observed this in one of his own cases.

Bone Marrow. This is essentially myeloid in structure, the great majority of the cells present being neutrophilic and eosinophilic myelocytes. Normoblastic foci are very numerous. The white nodule examined in one of the sections is found to be a necrotic area from which practically all the cellular elements have disappeared.

Sections of liver, spleen, and lymphatic gland, specially stained with methyl-violet, show the presence of a certain amount of amyloid change.

Remarks on the Nature and Diagnosis of Hodgkin's Disease. The present case is, therefore, as the examination after death proves, undoubtedly one of Hodgkin's disease, or, to give this disease some of its synonyms, lymphadenoma, lymphoma granulomatosum, lymphomatosis granulomatosa,[2] Hodgkin's granulomatous lymphoma,[3] Sternberg's lymphatic glandular disease,[4] granulomatosis textus lymphatici (Typus Paltauf-Sternberg),[5] lymphogranulomatosis (Paltauf-Sternberg),[6] malignant granuloma (granuloma malignum) of the lymphatic apparatus (Benda[7]), malignant granuloma with giant cells,[8] granuloma-like sarcoma of lymphatic glands.[9] The last name fits in best with those cases in which, on microscopic examination after death, the granulomatous growth is found to

[2] Fraenkel and H. Much, Zeitsch. f. Hygiene, Leipzig, 1911, lxvii, 159; see also Münch. med. Woch., 1910, lvii, 685.

[3] D. Symmers, Publications of Cornell Univ. Med. College: Studies from the Depart. of Path., 1909, vol. ix (separate pagination).

[4] J. Sailer, Philadelphia Med. Jour., 1902, ix, 615, 669; A. Sticker and E. Löwenstein, Centralbl. f. Bacteriol. etc., 1910, lv, 267.

[5] H. Lehndorff, Jahrb. f. Kinderheilkunde, 1908, lxvii, 130.

[6] E. Fabian, Wien. klin. Woch., 1910, xxiii, 1515, and Centralbl. f. allg. Path. u. path. Anat., Jena, 1911, xxii, 145.

[7] Verhandl. d. Deut. pathol. Gesellschaft, Jena, 1904, i, 123.

[8] Schwenkenbecher and Fischer, Abstract in Münch. med. Woch., 1911, lviii, 220.

[9] Dietrich, Deut. med. Woch., 1908, xxxiv, 1188.

have invaded bloodvessels,[10] as it did in the case of a man, E. F., aged twenty-seven years, who was under my care in 1905, and whose case I have elsewhere[11] described. Bone erosion from pressure in Hodgkin's disease[12] might clinically suggest a still greater degree of malignancy. The term pseudoleukemia, which has been widely employed in Germany as synonymous with Hodgkin's disease, is said to have been first introduced in 1865 by J. Cohnheim,[13] but it was apparently not intended by him as synonomous with Hodgkin's disease.[14] If the term pseudoleukemia is to be retained in medical literature, it should probably be reserved for those cases of so-called lymphosarcomatous, or, better, lymphocytomatous, infiltration of the kidneys, intestines, or other parts of the body, with small, round lymphocyte-like cells, which separate the cellular elements of the infiltrated part without destroying them, thus giving rise to a microscopic picture, exactly resembling that of lymphocythemic infiltration in lymphocythemia or lymphocytic leukemia, but unaccompanied by any lymphocythemic blood changes.[15]

It is highly probable that some of the supposed cutaneous manifestations of Hodgkin's disease have been really lymphocytic nodules in the skin occurring during an early (aleukemic) stage of leukemia. In some cases of Hodgkin's disease a pruriginous eruption develops, which may even progress to a condition of almost universal erythrodermia exfoliativa. The glandular swellings may then be wrongly supposed to be secondary to the cutaneous eruption.[16] In a case that I saw in private practice the itching was present several months before the glandular enlargement was observed.

There are no blood changes characteristic of Hodgkin's disease, but a polymorphonuclear leukocytosis is fairly often met with,[17] probably sometimes as a reaction toward counterinfections of various kinds. A relative increase of lymphocytes, "sign of Pinkus,"[18] probably more often occurs in the cases of pseudoleukemia (lymphocytomatosis or lymphosarcomatosis) to which I have already referred, and it is, of course, found[19] in early, so-called aleukemic stages of lymphocytic leukemia (lymphocythemia). Leukopenia[20] may occur, as proved by the present case, in late stages of Hodgkin's disease,

[10] Dietrich, Deut. med. Woch., 1908, xxxiv, 1188 Also W. T. Longcope, Bull. Ayer Clin. Lab. of the Pennsylvania Hospital, 1903, No. 1, p. 4; 1906, No. 3, p. 86; 1907, No. 4, p. 18.

[11] F. P. Weber, St. Bartholomew's Hosp. Reports, London, 1908 (for year, 1907), xliii, 81.

[12] W. B. Warrington, Liverpool Medico-Chirurgical Journal, 1911, xxxi, 53.

[13] Virchow's Arch., 1865, xxxiii, 451.

[14] D. Symmers, loc cit.

[15] Fürstenberg and Buchmann, Ziegler's Beiträge z. path. Anat. u. z. allg. Path., 1907, xlii, 447. F. W. Higgs, Proc. Roy. Soc. Med. (Children's Section), 1909, iii, 17. Sterling, quoted by Werdt, vide infra. F. P. Weber, Trans. Path. Soc., London, 1896, xlvii, 117, and Trans. Med. Soc., London, 1909, xxxii, 100, 101. H. Wehland, quoted by Werdt, vide infra. F. von Werdt, Frankfürter Zeitschr. f. Path., 1909, ii, 616; also Banti, quoted by Werdt, loc. cit.

[16] H. D. Rolleston, Brit. Med. Jour., 1909, ii, 852.

[17] E. Fabian, loc cit.

[18] E. Fabian, Deut. med. Woch., 1910, xxxvi, 261.

[19] F. P. Weber, loc. cit., see 11.

[20] E. Fabian, loc. cit.

when extensive fibrosis and necrotic changes have taken place in the spleen and lymphatic glandular apparatus of the whole body. Leukopenia must certainly not be regarded as a pathognomonic sign of splenic anemia or Banti's disease, if, indeed, splenic anemia can be regarded as anything more than a symptom complex, due to various causes, and Banti's disease as a late stage of that symptom complex characterized by the presence of cirrhosis of the liver with or without ascites. But to this question I shall return later.

Since Carl Sternberg's well-known paper (1898),[21] "On a peculiar Form of Tuberculosis of the Lymphatic Apparatus Presenting the Clinical Features of Pseudoleukemia," it has been generally acknowledged (1) that cases of tuberculous disease of lymphatic glands are not very rarely met with clinically, resembling Hodgkin's disease; (2) that tuberculosis occasionally occurs as a superadded infection in cases of Hodgkin's disease. In spite of Musser's[22] and Sailer's[23] summing up, I think that the work of Andrewes,[24] Reed,[25] Simmons,[26] Longcope,[27] Warnecke,[28] Muir,[29] Kidd and Turnbull,[30] and other writers abundantly proves the existence of Hodgkin's disease as a distinct disease or group of diseases with a characteristic morbid histology of its own, although the clinical and postmortem features may sometimes be masked by associated tuberculosis. I have elsewhere[31] discussed this association of Hodgkin's disease with tuberculosis, but I shall here shortly describe another striking example of such association.

The patient, Max L., aged forty-four years, was admitted under my care at the German Hospital on April 22, 1908, and the history of enlarged lymph glands dated from early in 1902. On admission, the spleen and liver could both be felt below the ribs, and there was much enlargement of the lymphatic glands in the neck, armpits, and groins. There were walnut-sized glandular clumps in the axillæ and considerably larger swellings in both inguinal regions, especially on the left side.

There was some ascites. A blood examination by Dr. Chapuis gave: Hemoglobin, 45 per cent.; red cells, 2,500,000 in the cubic millimeter; color index, 0.9. The white cells, especially the polymorphonuclear leukocytes, were greatly increased in number. Treatment by Röntgen rays, which had been previously tried elsewhere, atoxyl, etc., did no permanent good. The patient's general condition varied from time to time, and there were occasional

[21] Zeitschr. f. Heilkunde, 1898, xix, 21.
[22] Trans. Assoc. Amer. Phys., 1901, xvi, 638.
[23] J. Sailer, loc. cit.
[24] Trans. Path. Soc., London, 1902, liii, 305.
[25] Johns Hopkins Hosp. Reports, 1902, x, 133.
[26] Jour. Med. Research, 1903, ix, 378.
[27] W. T. Longcope, loc. cit.
[28] Mitteil. a. d. Grenzgebiet. d. Med. u. Chir., Jena, 1905, xiv, 275.
[29] Glasgow Med. Jour., 1905, lxiv, 161.
[30] Arch. Path. Inst., London Hospital, 1908, ii, 130 to 155.
[31] F. P. Weber, loc. cit., sec. 11; Lancet, London, 1904, i, 924 to 928. (Contains references to older literature on the relation of tuberculosis to Hodgkin's disease.)

periods of pyrexia. In June, 1908, there was still a large polymorphonuclear leukocytosis present; the white cells numbered 18,550 in the cubic millimeter of blood. A right-sided pleuritic effusion needed occasional tapping in September and October, 1908. In November, 1908, some diminution was noted in the size of the lymphatic glands in the right groin. There was still much leukocytosis, 28,000 white cells in the cubic millimeter of blood. In 1909 the patient suffered from increasing feebleness, emaciation, and dropsy, and died on February 21, 1909. At the postmortem examination and subsequent microscopic examination tuberculous lesions were found in the lungs, liver, spleen, and lymphatic glands, and a necrotic change, probably of tuberculous origin, was present in one of some whitish nodules from the bone marrow, which was red in color, of the shaft of the left humerus. But in the largest inguinal gland, kindly examined by Dr. J. C. G. Ledingham, the characteristic features of Hodgkin's disease were detected. It is by the way, perhaps, worth mentioning, that Calmette's ophthalmoreaction for tuberculosis had been tried in May, 1908, with a negative result.

The necrotic and lardaceous changes found after death in the viscera of some cases of Hodgkin's disease, as in the case of H. A., specially under consideration, by their resemblance to changes found in cases of syphilis, tuberculosis, and other microbic diseases, suggest that the exciting cause of Hodgkin's disease is a microbic infection of some kind. Similarly, the fibrotic and cicatricial changes which form so conspicuous a feature in the pathological histology of late cases of Hodgkin's disease are probably analogous to the conservative and limiting fibrosis of chronic tuberculous and tertiary syphilitic lesions. The microbic theory is likewise supported by the occasional occurrence of very acute cases, to examples of which I have elsewhere[32] drawn attention. Acute cases have also quite recently been described by A. T. Wilkinson,[33] J. Mitchell Clarke,[34] and Hirschfeld and Isaac.[35] But though the cause of Hodgkin's disease is almost certainly microbic, attempts at inoculation and cultivation have repeatedly given negative results. Pröscher and White,[36] indeed, in 1907, reported that, by the Levaditi and Giemsa methods of staining, they had succeeded in detecting spirochetes of some kind in human lymphadenomatous glands, but their results have not been confirmed by other investigators. Neither is the recent paper by Eug. Fraenkel and H. Much,[37] of Hamburg, very convincing. These observers claim that Hodgkin's disease, which they call lymphomatosis granulomatosa, is produced by granule-like

[32] F. P. Weber, loc. cit., see 11.
[33] Manchester Path. Soc., March 10, 1909; also Lancet, 1909, i, 920.
[34] Jour. of Path. and Bact., Cambridge, 1908, xiii, 92.
[35] Med. Klinik, 1907, iii, 1580.
[36] Jour. Amer. Med. Assoc., 1907, xlix, 774, 1115; also Münch. med. Woch., 1907, liv, 1868.
[37] Loc. cit.

bacteria (granules of Much), which are intimately allied to, if not actually a variety of, the Bacillus tuberculosis, and which are said to be stained by an intensified Gram method, and though not "acid-fast," to be resistant to antiformin. Here, I may mention that Sticker and Löwenstein,[38] who think that Hodgkin's disease is probably caused by bovine tubercle bacilli, claim that, by inoculation of material from cases of Hodgkin's disease in man, they have succeeded in producing a granulomatous tissue in guinea-pigs, which, although apparently free from tubercles and tubercle bacilli, nevertheless is capable of setting up obvious tuberculosis when it is reinoculated into other guinea-pigs. Obviously such results need much confirmation before acceptance.

In true Hodgkin's disease the lymphatic glands of some one region of the body are much more enlarged at first than the others, as if they constituted the primary focus or centre of the disease.[39] Not rarely, as in the present case of H. A., those on one side of the neck are chiefly affected at first; sometimes a group of retroperitoneal glands seems to be primarily involved;[40] in a case under my care in 1908 the disease commenced in the mediastinum,[41] and so it did in a boy, aged four years, whose case is one of those described by Kidd and Turnbull;[42] Douglas Symmers[43] has described a case which he regards as one of "primary Hodgkin's disease of the spleen." However, Symmers' case is by no means conclusive. The patient, a woman, aged eighteen years, died on the day following the operation of splenectomy, and the spleen was examined microscopically, but no postmortem examination of the other abdominal and thoracic contents was obtained. I believe that the disease, when it is localized in the mediastinum, as it was in a case of mine, to which I have just referred,[44] may give rise to a regular tumor-mass, not merely a conglomeration of lymphatic glands.

In the present cases (H. A.), as doubtless in several other cases, the superficial lymphatic glands, which at first formed a prominent tumor on one side of the neck, shrivelled up during the course of the disease so as to become hardly noticeable. The disease superficially appeared to be in process of cure, but in reality, the lymphatic glands in the thoracic and abdominal cavities and the lymphatic tissue of the spleen were becoming gravely affected. Something of the same kind is doubtless what happens in many cases in which more or less complete cure is supposed to have been affected by arsenical medication or by the action of Röntgen rays. As the disease progresses, the lesions of Hodgkin's disease tend to become more and more fibrotic and to lose their characteristic microscopic

[38] Loc. cit.

[39] F. P. Weber, loc. cit., see 11.

[40] W. T. Longcope, loc. cit. F. Warnecke, loc. cit.

[41] F. P. Weber and J. C. G. Ledingham, Proc. Roy. Soc. Med. (Clinical Section), 1909, ii, 66.

[42] Loc. cit.

[43] Loc. cit.

[44] Weber and Ledingham, loc. cit.

features. This is well illustrated by the present case (H. A.), and by one or two unpublished cases of which Dr. Ledingham has told me. Probably in most cases a counterinfection of some kind takes place at the end, and in the case of H. A. the presence of streptococci in the perivascular lymph spaces of lymphatic glands affords evidence of such a terminal infection.

With regard to clinical diagnosis in the present case, the negative results of Wassermann's seroreaction for syphilis and von Pirquet's cutireaction for tuberculosis were of some value, and leukemia was completely negatived by the blood picture. Hodgkin's disease may perhaps be simulated[45] by malignant disease of abdominal viscera (suprarenals) with secondary infiltration of lymphatic glands in the neck, but had there been any such abdominal malignant disease in the present case, one would have expected enlargement of the inguinal as well as of the cervical glands to have ultimately occurred; moreover, the diminution and almost complete disappearance of the cervical swelling would hardly have been likely, had it been due to carcinomatous infiltration. H. D. Rolleston[46] and others draw attention to the possibility of cases with splenic enlargement and pyrexia, suggesting a diagnosis of malaria or enteric fever, and, indeed, in the present case it was thought advisable to try Widal's reaction, but the result was negative.

In only a few cases of Hodgkin's disease does the patient's temperature chart help at all in the diagnosis. When there is any fever, it is mostly of an irregular kind with a moderate evening rise, but occasionally a long, regularly recurrent, periodic type of fever[47] is met with, the chronic relapsing pyrexia of Hodgkin's disease, which has been called the "Pel-Ebstein symptom," owing to the writings of Pel[48] and Ebstein,[49] in 1887. Of this, perhaps the most remarkable example in existence is an eight month's chart, recently recorded by C. H. Melland.[50] Such cases have even been labelled "Ebstein's disease." Less regular recurrent "pyrexial crises" are of rather commoner occurrence. During the pyrexial periods the superficial lymphatic glands are sometimes observed to swell, but they occasionally seem to diminish rather than increase in size, as in the case of Hodgkin's disease shown by Dr. J. Porter Parkinson before the Medical Society of London on March 27, 1911.

Wherever possible, the diagnosis of Hodgkin's disease should be confirmed at an early stage of the excision and microscopic examination of one of the enlarged lymph glands. Without the help of a biopsy it is by no means always so easy, as some probably suppose,

[45] H. D. Rolleston, personal communication. [46] Practitioner, 1911, lxxxvi, 496.

[47] F. de H Hall, Practitioner, 1911, lxxxvi, 473. L. Hofbauer, Wien. med. Woch., 1905, lv, 86. J. H. Musser, loc. cit. F. Taylor, Guy's Hosp. Reports, 1906, lx, 1.

[48] Berliner klin. Woch., 1887, xxiv, 644. [49] Ibid., 565.

[50] Edinburgh Med. Jour., 1911, New Series, vi, 156 to 164, Chart 1.

to distinguish Hodgkin's disease from chronic tuberculous or syphilitic enlargement of lymph glands. Many persons are doubtless alive and well today who would have been long since dead had the diagnosis of Hodgkin's disease pronounced on them been the correct one. Mistaken diagnoses in syphilitic and, especially, tuberculous cases doubtless account for many of the supposed cures of Hodgkin's disease. But that arsenical therapy (Fowler's solution, arsacetin, etc.) and the application of Röntgen rays can be of real use in many genuine cases of Hodgkin's disease there can scarcely be a doubt, even if a permanent cure cannot be effected. This consideration makes it very important that the diagnosis should be made as certain as possible by the help of a biopsy, so that arsenical medication may be carefully and methodically pushed, and *x*-rays perhaps also made use of. Mistakes in diagnosis in regard to the question of Hodgkin's disease have, however, sometimes, it must be admitted, been made, even after a biopsy and all other available methods. I may here mention that the great difference in regard to the ordinary progress of the disease between tuberculous lymph glands and the lymph glands of Hodgkin's disease furnishes another argument against the view that Hodgkin's disease is caused by any variety of the bacillus tuberculosis.[51]

A point of extreme clinical interest in the present case was the development of splenic enlargement and ascites, which, together with the subsidence and practical disappearance of the superficial lymphatic glandular tumors and the association of marked leukopenia with the anemia, produced the clinical picture of Banti's disease, that is to say, the stage of splenic anemia characterized by hepatic cirrhosis and ascites. So great, indeed, was the clinical resemblance, that the diagnosis of Banti's disease was actually arrived at by medical men who had not had an opportunity of seeing the case at an earlier period when the superficial glandular swelling in the neck was the most marked feature. The leukopenia may have been a result of the fibrotic and necrotic changes which involved so large a proportion of the lymphadenoid apparatus of the body.

Granting that there is a definite disease which may be termed splenic anemia, or, in its later stages, Banti's disease, I will now shortly consider a few of the conditions which may clinically simulate it.

Remarks on Various Cases Presenting the Clinical Picture of Splenic Anemia (Banti's Disease). Hodgkin's disease, or lymphadenoma, "with splenic predominance," as seen in the late stages of H. A., the present case, that is to say, a kind of splenic type of Hodgkin's disease, has been likewise called the Griesinger or

[51] Fraenkel and Much, loc. cit. J. H. Musser, loc. cit. J. Sailer, loc. cit. G. Sternberg, loc. cit. Sticker and Löwenstein, loc. cit.

lymphadenomatous type of splenic anemia, but Griesinger's original case, described by his pupil, Gretsel,[52] in 1866, was apparently not a certain one. The patient was a female child, aged only ten months, with great enlargement of the spleen and less enlargement of the liver, moderate rickets, and no leukemic blood changes. At the necropsy the lymphatic glands of the mesentery and retroperitoneal region were found enlarged, and Cohnheim, who examined the spleen microscopically, reported that it showed only hyperplasia of its normal constituents. There was a kind of fibrosis in the liver and kidneys. Griesinger's case cannot, therefore, with certainty be claimed as one of Hodgkin's disease in the modern sense of the term.

Leukopenia occurs in various conditions other than splenic anemia, conditions in which the spleen is chronically enlarged and has undergone extensive fibrotic or necrotic changes, and in which probably a great portion of the total lymphadenoid apparatus of the body is involved. I have already referred to the occurrence of leukopenia in the later stages of Hodgkin's disease. Leukopenia may occur in chronic malarial and syphilitic[53] disease of the spleen and liver.[54] Thus, S. S. Cohen and Rosenberger[55] drew attention to the occurrence of blood changes resembling those of Banti's disease in a case of splenomegaly apparently due to malaria. The connection of some cases of supposed Banti's disease with congenital or acquired syphilis has been suggested by Marchand[56] and others.[57]

Among hospital patients occasionally met with in London are sailors and various persons who give a history of having had malaria and having repeatedly visited or resided in hot climates, and who suffer from anemia with chronic splenomegaly, enlargement of the liver, doubtless a form of hypertrophic cirrhosis, and sometimes marked leukopenia.

In a man, M. C., aged twenty-five years, who had spent twelve years of his life in Jerusalem, where he had suffered a good deal from malaria, there was much enlargement of the spleen and considerable enlargement of the liver, slight jaundice, and anemia. While he was under my care at the German Hospital the number of his white corpuscles varied from 1200 to 4200 in the cubic millimeter of blood. His general health and appearance improved markedly and the jaundice disappeared.

A soldier, W. V., aged twenty-six years, was under my observa-

[52] Berl. klin. Woch., 1866, iii, 212.

[53] Leukopenia may likewise occur in splenomegaly due to primary tuberculosis of the spleen. In such a case described by P. Albrecht at a Viennese Medical Society (Wiener med. Woch., 1908, lviii, 2854) the white cells were counted at 3000 in the cubic millimeter of blood before the operation of splenectomy.

[54] L. d'Amato, Zeit. f. klin. Med., Berlin, 1905, lvii, 261.

[55] Amer. Jour. Med. Sci., Philadelphia, 1904, cxxviii, 271.

[56] Münch. med. Woch., 1903, l, 463.

[57] W. Schmidt, Münch. med. Woch., 1911, lviii, 625.

tion, in 1903, for enlargement of the spleen and liver, emaciation, anemia, slight albuminuria, and oozing of blood from the gums. He had lived for six years in India, where he had had attacks of enteric fever and malaria. He had been accustomed to a good deal of alcohol. When I saw him no malarial parasites were found in the blood and there was no leukemia. His white corpuscles varied between 3748 and 7180 in the cubic millimeter of blood. I heard that he died of "syncope" in September, 1903, and that there was a postmortem examination, but I could ascertain little more than that the spleen weighed 6½ pounds, the liver 10 pounds, and the heart 15 ounces.

In apparently similar cases the pathology and etiology may sometimes be very complicated. An example of this is the case of W. S., a fireman on a steamship, aged forty-two years, whom I showed to the Medical Society of London on April 8, 1907.[58] He gave a history of having taken a good deal of alcohol, of having contracted a chancre ten years ago, and of having suffered from fever, apparently malaria. He was anemic and the size of his spleen and liver was enormous. When at the German Hospital, in London, his white corpuscle count varied from 4160 to 10,000 in the cubic millimeter of blood. No malarial parasites were found, and some blood films from the liver were kindly examined by Captain W. G. Liston, I.M.S., for kala-azar parasites,[59] but with negative result. The patient afterwards went to a hospital at Stockholm, where he had to be tapped for ascites. A blood count made at Stockholm gave: Red cells, 3,500,000 in the cubic millimeter; white cells, 4300 in the cubic millimeter; polymorphonuclears, 70 per cent.; large lymphocytes, 16 per cent.; small lymphocytes, 12 per cent.; eosinophiles, 2 per cent.; hemoglobin, by von Fleischl's method, 50 per cent. He died in the hospital on May 19, 1908, and the Medical Superintendent, Dr. G. D. Wilkens, who very kindly wrote to me about the case, summed up the changes found at the postmortem examinations as follows: Fibrous pericarditis, with complete adhesion of the two surfaces; chronic fibrous myocarditis; acute pneumonia of the lower lobe of the right lung; hepatic cirrhosis; splenomegaly with fibrous induration and spots of pigmentation, possibly left by old malaria; tuberculous peritonitis; tuberculosis of the bronchial and periportal lymphatic glands.

A very interesting case of chronic malignant endocarditis simulating splenic anemia[60] came under my notice in 1909. The patient, G. W., was a sailor, aged twenty-eight years, who had contracted

[58] F. P. Weber, Trans. Med. Soc., London, 1907, xxx, 393.

[59] Cf. cases of hepatic cirrhosis due to the protozoal parasite of kala-azar, described by L. Rogers (Ann. Trop. Med. and Parasitol., Liverpool, 1908, ii, 147); also the cases of infantile splenomegaly with anemia, due to Leishman parasites, described by Nicolle, Jemma, Pianese, Gabbi, Feletti, Cannata, and others.

[60] F. P. Weber, Trans. Med. Soc., London, 1910, xxxiii, 83.

malaria in the Straits Settlements about four years previously. When seen in London, however, he presented no signs of active malaria, and had already been treated at several London hospitals, where apparently the diagnosis of splenic anemia had been made. At the German Hospital he was extremely pale, weak, and wasted, and there was a tendency to bleeding from the gums. His spleen extended downward into the inguinal region, and his liver was likewise enlarged and hard. His legs were pigmented as a result of a chronic petechial eruption, and there were a few minute hemorrhages in the skin of the arms and trunk, in the conjunctivæ, and in the retinæ. There was great anemia with leukopenia. Red cells, 1,700,000 in the cubic millimeter of blood; white cells, 1200 to 1900 in the cubic millimeter; hemoglobin, 30 to 35 per cent. The heart was somewhat enlarged and there was a systolic apical murmur. The necropsy showed the presence of chronic malignant endocarditis, and a microscopic examination by Dr. J. C. G. Ledingham of pieces of the spleen, liver, kidney, and bone marrow from the shaft of the humerus, showed, in all four organs, as their most conspicuous pathological histological feature, a plasma cell development with the elaboration of new fibroblastic tissue.

Perhaps, after all, in the present state of our knowledge, splenic anemia, with its later stage, known as Banti's disease, is best looked upon as a symptom group, which may be set up by various pathogenic agencies, the nature of some of which is known, though that of others has not yet been discovered.

In quite a considerable number of cases presenting during life the clinical features of splenic anemia, old thrombotic obstruction of the splenic and portal veins, with sometimes more extensive recent thrombosis as well, has been discovered after death. For examples of that kind we could refer to the published cases of Dock and Warthin,[61] 1904, Oettinger and Fiessinger,[62] 1907, Edens,[63] 1907, F. Dévé,[64] 1908, and several others; occasionally the splenic artery has been found diseased. In some of these cases the splenomegaly was doubtless secondary to the obstruction in the splenic and portal veins, but in other cases the vascular disease may have been secondary to a toxemia of splenic origin.

Cases of biliary cirrhosis of the liver, Hanot's type, with splenomegaly,[65] are, owing to the chronic jaundice, seldom likely to be diagnosticated as cases of splenic anemia. The Gaucher type of primary splenomegaly[66] is scarcely ever met with. But there are certain cases of congenital or acquired chronic acholuric, so-called

[61] Amer. Jour. Med. Sci., Philadelphia, 1904, cxxvii, 24.

[62] Revue de Méd., Paris, 1907, xxvii, 1109.

[63] Mitteil. a. d. Grenzgebieten d. Med. u. Chir., Jena, 1907, xviii, 59.

[64] Normandie Médicale, March 1, 1908; abstract in Arch. des Maladies du Cœur, etc., Paris 1908, i, 606.

[65] F. P. Weber, Trans. Path. Soc., London, 1903, liv, 103.

[66] Weber and Dorner, vide infra.

hemolytic jaundice, with splenomegaly and anemia,[67] which might, owing to the temporary or permanent absence of obvious clinical jaundice, be mistakenly labelled as examples of splenic anemia. Such cases might be headed splenomegalic anemia or splenomegalic hemolytic anemia, acquired or congenital, to avoid the confusion with splenic anemia.[68] In a paper,[69] with Dr. Dorner on "Four Cases of Congenital Acholuric Jaundice in One Family," we wrote: "It is highly probable that in some cases of the disease the jaundice, at all events, obvious jaundice, may be intermittent instead of remittent, that is, that for a time at least jaundice may be apparently absent, though the splenomegaly and characteristic blood features of the disease are present. Such cases might be clinically termed cases of splenomegalic anemia. . . . In other words, it appears almost certain that a form of splenomegalic anemia without jaundice may occur, although, perhaps, only temporarily, as an incomplete form of the chronic splenomegalic acholuric jaundice, of which the family in question affords complete examples."

In conclusion, I must specially thank Dr. Daser for his information on the early history of the patient H. A., Dr. Dorner for his help in the examination of the same case at the German Hospital, and Dr. Ledingham for his kind report on its pathological histology.

THE INSIDIOUS ONSET OF PNEUMOTHORAX.[1]

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It is unnecessary to attempt to enter here into a detailed description of pneumothorax, its etiology, symptoms, or treatment. This condition is so well known nowadays, and its recognition, despite its protean symptomatology, so well established by the enormous amount of work and the multitudinous articles on this subject, that anything further seems superfluous. There is, however, a certain type of case in which pneumothorax seems to be quite frequently overlooked. I refer to those instances in which the pneumothorax develops insidiously, without the classical signs of sudden pain and intense dyspnea. A pneumothorax developing

[67] F. P. Weber, Amer. Jour. Med. Sci., Philadelphia, 1909, cxxxviii, 24; F. P. Weber and G. Dorner, Lancet, London, 1910, i, 227.

[68] Armand-Delille, Soc. de Pédiatrie, Paris, June 23, 1910. Armand-Delille and Feuillée, Soc. méd. des Hôpitaux de Paris, February 2, 1909. Chauffard and Troisier, Soc. Méd. des Hôpitaux de Paris, February 19, 1909. R. Hutchison, Case of Splenomegaly, shown at the Clinical Section of the Royal Society of Medicine, March 10, 1911.

[69] Weber and Dorner, loc. cit.

[1] Read before the Section on General Medicine of the College of Physicians, April 24, 1911.

slowly or silently without symptoms tends to escape notice, and especially if it occurs in an apparently healthy individual, or, less excusably, in the presence of active pulmonary tuberculosis, the signs of which may obscure the findings. Furthermore, the very type of pneumothorax which is most difficult to detect is also most liable to develop insidiously. It is obvious that a small circumscribed partial pneumothorax will not only give less clear physical signs, but also fewer symptoms. It is the insidious development of pneumothorax that I wish especially to emphasize, and I have chosen such cases to report as I hope will illustrate this.

The first case to be reported is from Dr. Alfred Stengel's service at the University Hospital:

Case I.—M. R., white, male, aged twenty-three years, car conductor, was admitted on December 1, 1903 with the following history: Present illness began last winter, with a "heavy cold" in chest. Patient had only cough and general weakness, but was compelled to give up work at intervals of a few days or weeks, until about three months ago, when he had to give up entirely. He had slight pain in chest at times, but it was not a prominent symptom. Dyspnea had been the worst symptom for about three months. He had lost about twenty pounds in weight since last winter. At times he expectorates large amounts of sputum, but usually very little. In the summer of 1903 he had on several occasions hemoptysis, at times quite profuse and again slight.

On admission his complaints were cough, weakness, pains in left chest, and dyspnea. Temperature, 99°; pulse, 105; respirations, 26. The physical examination of his thorax is recorded as follows: "Left shoulder carried higher than the right. Chest seems flattened. Left side seems larger than right, and measurement shows a difference of nearly 1 inch, the right measuring $16\frac{1}{2}$ inches and the left $17\frac{1}{2}$ inches just above the nipples. Expansion greater on right; the left side expands very slightly, if at all. No fremitus on left side. There is a tympanitic note over the upper part of the left thorax; anteriorly, flatness begins at the fourth rib, posteriorly at the third spine. The dulness is movable. On the right the lower border of resonance is at the sixth rib anteriorly, and posteriorly at the eleventh spine. No breath sounds heard on the left side; on the right side the breath sounds are puerile. All the signs of pneumothorax are present on the left side. The heart: The apex beat is palpable in fifth interspace, just about $\frac{3}{4}$ inch inside right nipple line. A pulsation is visible in the third, fourth, and fifth interspaces on the right side. The heart border is inseparable from flatness of fluid on the left side. The cardiac sounds are loud, and there are no murmurs. The remainder of the physical examination was of no importance. The laboratory examinations showed a moderate leukocytosis, but never revealed the presence of any tubercle bacilli on repeated examinations. The future course of the case showed

little change, save that the fluid continued to increase until the pneumothorax was almost replaced by it; finally, a thoracentesis was performed, with the evacuation of forty-two ounces of thick grayish fluid, which produced tuberculosis when injected into guinea-pigs. The patient eventually left the hospital in a much improved condition. Dr. Stengel's last note on the case is as follows: "Points especially worthy of note are: (1) The gradual development of pneumothorax—this method of development I have noted in five out of six cases seen during the past eight months; (2) entire disappearance of the air, with replacement by fluid, speaking for a healing of the rupture, and subsequent absorption of the air; (3) the failure to find tubercle bacilli."

Thus, we have here a case of tuberculosis, as proved by inoculation, with a left-sided pneumothorax developing insidiously, which at first presented the classical signs known as Laennec's pneumothoracic tripod—tympany, absence of fremitus, and absence of breath sounds. As the increasing fluid encroached upward the diagnosis became more difficult, and the possibility of confusing the tympany of the pneumothorax with the skodiac note of a "tympany by mediate relaxation" became greater, this confusion, of course, being decided by the auscultatory phenomena. The displacement of the heart in this case was very great, and its return to a more normal position after thoracentesis very striking.

Another case developing insidiously a pneumothorax in the course of a pulmonary tuberculosis was seen by me in the University Hospital medical dispensary shortly after I had commenced to study this condition, and I am sure that my diagnosis of it was in large measure due to the freshness of the subject in my mind. The diagnosis was agreed in by Dr. R. G. Torrey, and confirmed by skiagraph. The case is as follows:

Case II.—J. W. M., colored, aged thirty-six years, came to the dispensary complaining of cough, pains in chest, and loss of weight. The history of the present illness dated back several months, at which time he developed a cough, which persisted, and two months before we saw him he commenced to lose weight, feel feverish, and have occasional pains in his left chest, and mild dyspnea. No history could be obtained of any sudden attack of pain or dyspnea. The patient was clearly in the last stages of tuberculosis, and examination of his lungs revealed extensive involvement on both sides. In addition, on the left side an area of hyper-resonance was met, which commenced above at the second rib, and extended down, slightly overlapping the heart, and outward to the axilla and the lower part of the posterior aspect up to the tip of the scapula. The note was less hyper-resonant just below the nipple, but in the axilla became loud and booming. Over this area fremitus was almost lost, and the breath sounds were distant bronchovesicular in character. Voice sounds were loud and egophonic in character.

No metallic tinkle or succussion splash could be heard. The stereoscopic skiagraphs taken by Dr. Pancoast show a marked tuberculous involvement of both lungs. The right shows no cavity. The left shows a pneumothorax of the whole lower part of the pleural cavity, being bounded by the heart to the right, above by the second rib anteriorly, and posteriorly extending up to the angle of the scapula. The pneumothorax is crossed in front by a band of adhesions or a marked pleural scar at the level of the fifth rib. These pictures are beautiful, and demonstrate the value of the stereoscopic method, since from neither plate separately could the diagnosis have been made with certainty, but when examined in combination the resulting picture was unmistakable.

The patient was sent to the Rush Hospital under the care of Dr. T. Mellor Tyson, and died there twenty-three days later.

We have here to deal with a partial pneumothorax of tuberculous origin developing insidiously in a case of active tuberculosis. This case is in many respects typical of its kind. Tuberculosis furnishes the vast majority of cases of pneumothorax, and of the stages, it is the active in which this condition is most prevalent. Partial pneumothorax can occur only in such cases as have adhesions already present to prevent its becoming total, and it is in partial pneumothorax that an insidious onset is most frequent. All these conditions were present in this case.

A most exhaustive study of partial pneumothorax has been made by Jaccoud, who classifies them on an anatomical basis, first into superior and inferior, and the inferior again into anterolateral, posterolateral, and of the whole circumference. It is under this latter class that our case should be placed. Of course, the shape, position, and extent of a pneumothorax are entirely dependent on conditions in the pleural cavity, such as adhesions or obliterations.

A third type of case with insidious onset is well illustrated by the following case. I cannot do better than quote verbatim the notes Dr. Stengel gave me concerning this patient:

Case III.—H. La., aged thirty-six years. His previous medical history was uneventful. Was visiting Philadelphia in December, 1903, when he contracted a severe cold, or influenzal bronchitis. His cough was severe, but not productive, and he felt quite depressed and "grippy." He was not conscious of any special oppression, dyspnea, or thoracic pain, and first consulted Dr. Stengel because some of his friends thought he was neglecting a bad cold. Upon physical examination it was found he had partial pneumothorax of the right side. The physical signs—tympany, amphoric breathing, and coin test—were found in the part of the chest midway between the base and apex, and were quite marked. The patient was sent to the University Hospital for rest and care. Within the next twenty-four hours the whole pleural sac became distended with air, and some displacement of the heart toward the left took place.

Soon after this metallic tinkling developed, and after a few days a moderate effusion of liquid was demonstrable. The latter never increased greatly, and at no time rose above the level of the fifth rib in front. Hippocratic succussion was pronounced when the fluid was at its height. The patient was in the University Hospital from December 11, 1903, to January 8, 1904, and was subsequently under observation outside the hospital for another month. During this entire time his temperature was constantly subnormal, and without marked diurnal variations; the pulse rate was never above 90, and much more commonly below than above 80; the respiration rate varied between 20 and 26. After the first few days all cough subsided, and never subsequently recurred. Repeated examinations failed to show any indications of a pulmonary lesion; the superficial glands were not enlarged, and the patient's general nutrition improved steadily from the day he took to bed. The pleural effusion was absorbed within two weeks after its appearance, and soon after this the amphoric breathing ceased, indicating a probable closure of the pulmonary rupture or fistula. This was speedily followed by diminution of the pneumothorax, and within a month by its complete disappearance. The patient was repeatedly examined after his recovery, and no indications of a pulmonary lesion could be detected. He is at this date in perfect health. The most surprising features in this case were the insidious development of a complete pneumothorax, and the absence of marked subjective symptoms affecting either the circulation or respiration, and the absence of discomfort of any sort, which is witnessed to by the patient's utter lack of realization of his condition, and is more remarkable in view of his being himself a well-trained physician. The failure to detect any evidence of tuberculosis of the lungs at the time of the illness and the absence of such during the intervening seven years confirms the diagnosis made at that time of pneumothorax, due to rupture of a superficial air vesicle during a paroxysm of coughing.

These three cases just reported will serve to show the occurrence of pneumothorax, both partial and complete, with insidious onsets under varying conditions. This type of onset is obviously not infrequent, and the large number of cases in which unsuspected pneumothorax is found at autopsy makes it certain that it is quite a common happening. Every author writing on this subject of recent years recognizes both types of onset, and quite a number, among others Emerson,[2] in his monograph, and James,[3] in Osler's *Modern Medicine*, quote the figures of Saussier in his Paris *Theses*, 1841, to the effect that in 196 cases reported there were 68 with sudden onset. At first sight these figures appear remarkable, and

[2] Johns Hopkins Hospital Reports, vol. xi, p. 434.
[3] James, Osler's Modern Medicine, vol. iii, p. 875.

it would be discouraging for us to have to believe that seventy years ago clinicians were recognizing three times as many insidious pneumothoraces as of those developing suddenly. However, Emerson, in the same monograph, several times speaks of Saussier as having been able to collect only 169 cases, and this suggested a possible error. A glance at the original thesis showed the trouble. On page 6 Saussier says: "Les observations sur les quelles mes recherches sont appuyées se montent a 169 et ont été recuillies à une foule de sources;" and later, on page 68: "Les symptomes du pneumothorax ou de la perforation ont paru subitement ou d'une manier lente dans 196 cas ou on a pris la peine de les indiquer, savior: 68 fois d'une subsite et 28 fois d'une manier lente." It is an apparent typographical error, which turns 96 into 196.

Thus, instead of his figures showing a sudden onset in 68 out of 196 cases, they really show a sudden onset in 68 out of 96, or in more than two-thirds of the cases. There is no question that this is the proper interpretation of his figures, since the sum of 68 and 28 is 96; and since having been able to collect only 169 cases, he would scarcely say that in the 196 cases in which the trouble was taken to indicate the onset there were 68 sudden and 28 slow.

This unfortunate author has been quoted from generation to generation throughout medical literature in such a way as to precisely reverse his actual findings, and to complete his discomfort, his name in Osler's *Modern Medicine* is misspelled.

It has seemed worth while, therefore, to collect the figures in a series of cases concerning the type of onset. Of course, no statistics on such a point are free from criticism, especially if culled from the literature, for certain factors determine which cases shall be recorded. However, the number of cases obtainable is so large, and certain individual reports are of such considerable numbers, that the figures are surely approximate.

In the literature of pneumothorax there occur several extensive monographs, and of these the most recent and satisfactory is by Emerson, published in 1903. In this work Emerson gives abstracts of some 358 articles on this subject, and I had hoped at first to be able to collect a sufficient series of cases from those abstracts; but this proved to be impossible, as but few of them detailed the histories of the cases reported. I was therefore obliged to refer directly to the original articles in the majority of instances. Over 1500 cases were reviewed, being found in 180 references in the literature from 1841 to the present time. Of these 1500 cases, 500 were found which gave perfectly satisfactory and sufficient histories of the onset. Every doubtful case and every case which had been subjected to trauma or tapping was omitted. With regard to the onset only two groups were made, sudden and insidious, and the cases were found to be divided as follows: 385 sudden and 115 insidious, adding to a total of 500. These figures expressed in percentages give 77 per cent. sudden and 23 per cent. insidious cases.

This percentage does not probably represent the number of cases with insidious onsets for several reasons: (1) Many cases of pneumothorax with insidious onset are not recognized; (2) fewer of the cases with insidious onset are reported, and (3) many cases with a probable insidious onset had to be ignored on account of insufficient history, whereas in no case of sudden onset would the author fail to mention this striking feature. Nevertheless, the statistics are better than none or incorrectly quoted ones.

In looking over the mass of literature on this subject, many interesting points presented themselves; among others, the fact that there is no relative increase in the cases with insidious onset reported of recent years, as might be expected, and that the figures just quoted, representing almost the entire literature, vary but little from Saussier's true figures collected seventy years ago.

Another point which cannot be overlooked is the large number of cases reported in which a pneumothorax followed tapping of the pleural cavity. The early writers did not emphasize this possibility very strongly, and Biach,[4] in 1880, could find only 3 cases with this etiology out of the 918 he studied. More recently, however, several authors have reported larger numbers. Emerson in 1903 mentions 10 cases out of the 49 he reports, and Ayer,[5] out of 72 cases of pneumothorax, finds that 14 surely followed tapping, while 9 additional ones may have been similarly caused. The actual cause of pneumothorax following aspiration is in many cases obscure, and a number of possible explanations have been suggested: (1) Faulty technique, permitting air to enter from outside; (2) wounding of the lung, with the needle; (3) negative pressure may cause the rupture of an emphysematous bleb, or hasten the breaking through of a tuberculous cavity, or adhesions may lead to a tear of the visceral pleura; (4) gas may be liberated from the blood to fill the vacuum; (5) local respiration of the tissues. However fanciful some of these may seem, it appears incredible that faulty technique can be responsible for so many cases as are quoted above by Emerson and Ayer from such institutions as the Johns Hopkins Hospital and the Boston City Hospital. It is, of course, possible that the tympanitic note which is found so frequently over the upper part of the lung after aspiration, and which is usually interpreted as a skodaic note due to relaxation, although no perfectly satisfactory explanation has as yet been advanced, may be the cause of confusion in certain of these cases. I have examined the notes of a large series of cases of hydrothorax tapped at the University Hospital, and have found only one sure case of resulting pneumothorax and a few doubtful ones. A final point in this relation is the remarkable absence of intense symptoms in pneumothorax thus produced, probably

[4] Wien. med. Wochenschr., vol. xxx, No. 1, p. 6.

[5] Boston Medical and Surgical Journal, vol. clxiii, No. 13, p. 501.

explained by the fact that the lung on the affected side was already only partially functionating, owing to compression, by the effusion for relief of which the aspiration was performed, and that respiratory compensation had been established.

As a contrast to the third of the cases I have just reported, which was a total pneumothorax developing insidiously in an apparently healthy man, I wish briefly to mention the following, for the use of which I am indebted to my brother, Dr. William Pepper:

Case IV.—M. G., white, aged twenty-nine years, single, minister, was first seen on December 25, 1905, complaining of dyspnea and pain in the epigastrium. He gave the following history:

"Five days before admission, while smoking a cigar, the first tobacco he had smoked since a boy, he had a sharp, shooting pain about the middle of the sternum, lasting only a second. He stopped smoking, and was perfectly comfortable until the next day. While on a train he had a similar attack of pain, slightly more on the left side of the chest. This lasted for about one hour, during which time, after he left the train, and while walking, he was quite dyspneic. That evening and night he had considerable pain in the epigastrium and along the spine, and also an oppressive sensation over the chest. On Tuesday his bowels became constipated, and the pain increased over the whole abdomen, and continued along the spine. The next day he was quite comfortable until late in the afternoon, when he had a sharp pain over the whole left chest, with cramp-like pains in stomach and bowels. He was very dyspneic. The pain in the back had shifted to the left loin region, and was dull and aching in character; he had not slept the previous night on account of pain and shortness of breath. The pain in the chest had been relieved."

He was in perfect health at the time of this onset.

Physical examination revealed an almost complete pneumothorax of the left side. The signs were very clear; the left chest was fuller, and moved less on respiration than the right; fremitus was absent on the left side, and percussion gave a hyper-resonant note, less marked at the apex. The normal cardiac dulness was lost, being replaced by hyper-resonance; the cardiac dulness was found to the right of the sternum, extending $1\frac{1}{2}$ inches. Over the left side auscultation revealed cavernous breathing, metallic in character, and the voice sounds were also metallic. Metallic tinkling was occasionally heard, and the coin test was positive. In short, the signs of pneumothorax were all present and typical. The presence of cavernous breath sounds, while perhaps not so characteristic of this condition as absolute silence, is frequently seen, and should not be permitted to militate against a diagnosis of pneumothorax. The findings on the right side were normal in every respect.

The patient was only moderately dyspneic, with a normal tem-

perature, a pulse of 128, and respirations of 28 to the minute, which, however, rose suddenly two days after admission to 44, and then ran a varying course between 30 and 40. The patient remained under observation for two months, during which time the signs in the lungs varied greatly. The notes on the case are very full, and it deserves more study than can be given here. Briefly, the signs of pneumothorax gradually disappeared, and after recovering from a complicating bilateral phlebitis of the long saphenous veins the patient was apparently restored to his former good health. The sputum was repeatedly examined, but no tubercle bacilli were found, and no evidence of any tuberculous process in the lungs discovered. The etiology of this peculiar case remains a mystery, as does also that of the previous case. They both belong to that well-recognized group of spontaneous pneumothorax occurring in apparently healthy individuals.

Since it is my desire merely to emphasize the frequency of insidiously developing pneumothoraces, and since the rest of the cases which were found do not add anything to those already quoted, a detailed account of them seems unnecessary here. In conclusion, let me say that if the figures collected and quoted above truly represent the frequency of recognized cases with these two types of onset, we are forced to the admission that a great number of insidiously developing pneumothoraces are escaping notice. This is true even if we rule out those which are clinically unrecognizable, owing to their small size or position. There is no condition which in its symptomatology more closely obeys the laws of physics and the mechanical principles involved in physical diagnosis, and surely this condition should be consistently diagnosticated by careful physical examination without the necessity of having an alarming sudden onset to direct attention to it. In a later paper I shall discuss the occurrence of partial pneumothorax, a form which, as has been said, is particularly liable to escape notice.

It was some months ago that Dr. Alfred Stengel suggested to me that it might be profitable to look up the cases of pneumothorax which had occurred in his service at the University Hospital, and although I have more or less wandered from the original intent, yet I wish gratefully to acknowledge his suggestion and the use of his cases in this paper.

OBSERVATIONS ON SOUND PRODUCTION AND SOUND CONDUCTION ALONG THE RESPIRATORY TRACT.

By Joseph H. Barach, M.D.,
PITTSBURG.

In a preliminary communication[1] on the transmission of sound by the bony framework of the thorax and by adjoining osseous structures, I called attention to the tubular-like breathing which is to be heard during the respiratory excursion at certain named areas not previously considered.

Up to the present time the chief claim that those observations may have upon our interest is that they are striking examples of the sound conducting ability of the bony framework of the body, particularly the thorax, and as such, will necessarily direct our attention to a more extensive consideration of the relationship between the various auscultatory phenomena, their manner of production, and source of origin.

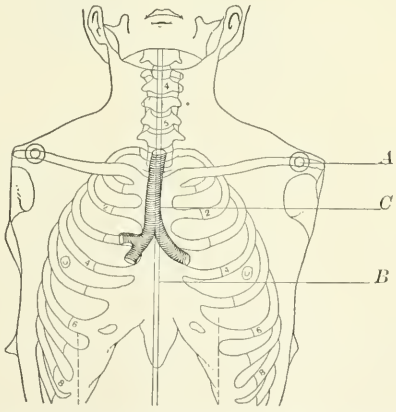

Fig. 1.—A, acromion area of bronchial breathing; *B*, median line of the body; *C*, position of the trachea as compared with the median line of the body. (J. C. Blake, Amer. Jour. Med. Sci., 1899.)

My first communication dealt chiefly with the finding of (1) tubular breathing at the acromial end of the clavicle; (2) tubular breathing over the uppermost portion of the spine—this sound I now wish to designate as cavernous breathing (*vide infra*); and (3) cavernous breathing also heard over the occipital and other bones of the cranium (Figs. 1 and 2).

[1] The Role Played in Auscultatory Signs of the Respiratory System by the Sound-conducting Property of the Bony Framework of the Thorax.—Amer. Jour. Med. Sci., December, 1910.

On first hearing this sound one may object to the term "cavernous" as applied here, yet the sound is a true cavernous sound, and such objections are therefore not valid.

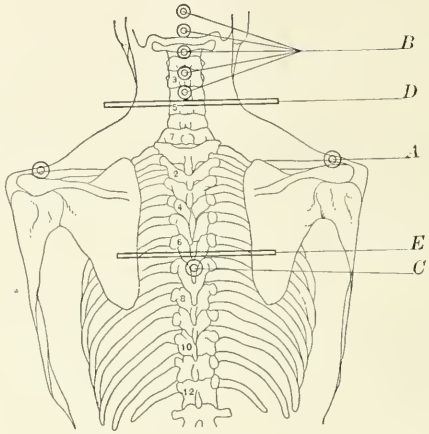

FIG. 2.—*A*, bronchial breathing heard over the acromion area: *B*, cavernous breathing heard above the recognized height; *C*, bronchial breathing heard below the recognized height; *D*, level of the fifth cervical vertebra where bronchial breathing is supposed to end; *E*, level of the fifth dorsal vertebra where the bronchial breathing is supposed to end.

SOURCES OF THESE SOUNDS.

Since up to the present we have only concerned ourselves with respiratory sounds heard from within the thorax proper, and rarely over the trachea, and since the generally accepted theory is that all sound production begins at the larynx, and also finding that bones are such excellent conductors of sound waves, it was a natural inference that the sounds heard at the above-mentioned areas had their beginning in the larynx and trachea.

This was the view accepted at the time of the communication referred to. But further investigations upon the origin and transmission of these auscultatory findings prove that sound production does not begin at the larynx, and that other factors, to be here considered, play a distinct role in determining the quality and quantity of sound heard.

In Fig. 3 I have arbitrarily divided the course of the upper air passage into spaces *A*, *B*, *C*, and *D*, representing the nasal fossa, the oral cavity, the laryngeal space, which includes the larynx and the trachea. Each of these represents an element in sound production and will be here considered.

Space *A*. The nasal fossæ are bounded above by a roof composed of portions of the nasal, frontal, ethmoid, and sphenoid bones and the basilar process of the occipital bone. The floor is formed by

the palatal bones, the outer walls by bones of the face, and the entire space is divided by a bony and cartilaginous septum.

Here we have an irregularly triangular space, bounded by bony walls and divided by a septum. Through this divided chamber passes a volume of air (about 500 c.c.) with each respiratory act, under constant pressure. The friction thus caused along its walls, including the turbinate shelves, necessarily sets up sound vibrations. These vibrations are taken up by the bones which enter into the formation of the walls of this bony cavity, and over some of them the sounds named are to be heard.

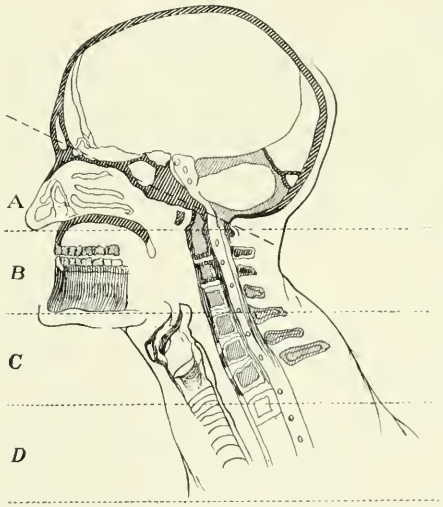

FIG. 3.—Upper air passage divided into the nasal fossa, *A*, the oral cavity, *B*, and the laryngeal and tracheal spaces, *C* and *D*.

Space *B*. The bony elements which may influence the production of sounds under consideration in this space are the teeth, the hard palate, and the posterior wall of the pharynx, which is composed of the cervical vertebræ. A volume of air on inspiration, passing with a definite amount of friction against the teeth, the hard palate, and striking the posterior pharyngeal wall, is certain to create a considerable number of sound waves.

Compared with space *A*, space *B*, as will be shown, plays a less important part in the sound production with which we are here concerned.

Space *C*. In this space lies the important organ of voice production, the larynx. Its cartilaginous walls, their peculiar arrangement, the positions and vibrations of the vocal cords make this organ an important source of sound vibrations, subject, however, within limitations to certain influences.

Space *D*. In this space lies the trachea, which, by virtue of being a cartilaginous and membranous tube, with an interior which has an undulating surface, itself forms an efficient excitor of sound waves. Its large share in sound production also enters into this consideration.

From what has been thus far stated, it is obvious that I regard spaces *A* and *B* of sufficient importance to warrant a consideration of the influence which they have upon auscultatory phenomena of the chest.

CONDITIONS MODIFYING SOUNDS.

Over the occipital area, nasal breathing, mouth closed. By applying the bell of a stethoscope (about the size of the Ford stethoscope) to the occipital bone, below its protuberance, one hears a pure type of cavernous breathing. The expiratory is louder than the inspiratory sound. The reasons for this are, I believe, that the outgoing volume of air strikes the roof of the nasal fossa more directly and more forcibly, and it may also be largely due to the position of the vocal cords, which are closer and vibrate more during expiration.

Mouth Breathing, Nostrils Closed. Without removing the stethoscope, and having the subject open the mouth and at the same time close the nostrils, one will find that the cavernous respiratory sound has almost disappeared.

The reason for this is, that the source of origin of the sound, the nasal fossa as a resonating chamber, has been eliminated. A distant and weaker sound is, however, still heard, and its origin may be from one of two or perhaps from both sources. It may be the faintly transmitted sound from that portion of the spinal column which gets its sound from the larynx, or it may be produced by the moving air in space *B* striking the posterior pharyngeal wall and at the same time setting in motion the residual air in space *A*, creating lesser sound waves and fainter sounds.

Mouth Breathing, Nostrils Open. Having the mouth and nostrils both open gives, on auscultation at the same areas, a louder sound than when the nostrils are closed, but a sound not nearly so large in volume nor high in pitch as when the mouth is closed.

Influence of Nasal and Oral Breathing upon Laryngeal and Tracheal Sounds. Sounds heard when auscultating over the larynx, trachea, manubrium sterni, and acromial ends of the clavicles, are much influenced by opening and closing of the mouth. With nasal breathing, when the nasal fossa acts as a reasonating chamber, the characteristic and familiar "bronchial" breathing is plainly audible. Closing the nostrils and opening of the mouth, thus eliminating the nasal resonator, reduces the volume and pitch of sounds at all of the above-named areas.

Heretofore it has been generally conceded that the production of sound heard over the respiratory organs begins at the larynx. The foregoing observations seem to prove conclusively that a definite amount of sound is created before the larynx is reached. Also that on eliminating the nasal resonating chamber, the various respiratory sounds become weaker, thus showing that the nasal resonator actually does add to the "sound total."

Part Played by the Larynx. During inspiration the downward moving volume of air, carrying with it a certain amount of sound acquired in the nasal resonator, reaches the larynx and there takes up more sound. During expiration, the upward moving volume of air, already charged with sound waves, enters the nasal resonator and there reverberates. So that the column of air which is to enter the larynx at both inspiration and expiration, already is carrying an appreciable amount of sound, and here receives more. How much more, and what actual part the larynx itself plays in the production of auscultatory sounds, I have attempted to determine by studying the physical signs in two tracheotomy cases.[2]

One of these breathed through a tracheotomy tube, and the other through a large tracheal fistula. Here the larynx took no actual part in sound production.

Case I.—Tracheotomy tube inserted at the second and third cartilages.

Over Cranial Bones. When patient was breathing through the tracheotomy tube only, having closed the nares and mouth, no sounds could be detected at the occipital area, nor anywhere above the level of the tracheotomy tube. Leaving the nose open, which permitted the passage of a limited amount of air through the nasal resonator, was followed by loud cavernous breathing over the entire head and upper portion of spinal column down to the level of the tracheotomy tube. The sounds were almost as distinct over the frontal bone as over the occipital and parietals.

Over Trachea. When the nares were closed and the nasal resonator entirely eliminated, the tracheal sound was softer than when the nares were left open and a small amount of air could pass through the nasal fossa which acted as a resonating chamber.

Over Sternum. At the manubrium sterni, when the patient breathed naturally and air was rushing in through the tracheotomy tube, and some through the nasal fossa, the usual "bronchial" sound was heard. The expiratory and inspiratory sounds were nearly of equal length. Closing of the nares, thus eliminating the nasal resonator, was followed by a weakening of the sounds, of which the expiratory was considerably louder than the inspiratory sound, probably because of backward reflection of sound waves in the trachea resulting from obstruction by the tube.

[2] Through the kindness of Dr. Chevalier Jackson and Dr. Ellen J. Patterson, I was afforded the opportunity of studying these cases.

At the Acromion Areas. With the nares open, and nasal resonator acting, the transmitted bronchial breathing was clearly heard with equal strength on both sides. Closing of the nares made the sound faint and almost inaudible.

In my first communication on this subject I called attention to the fact that the bronchial breathing over the right acromion area was louder than on the left, and also that by auscultating with the median line as a starting point, the tracheal sounds over the manubrium sterni and apices extended to the right side. This observation I have since been able to confirm in the greater number of my examinations, but not in all. Whether in those individuals in whom the acromion sounds are of equal values the trachea is situated nearer the median line, I am at present unable to say.

Right Apex Anteriorly (Bowles' stethoscope). Nose open, vesicular sound quite distinct; nose closed, no sounds.

Left Apex Anteriorly. Nose open, vesicular sound clear; nose closed, sounds very faint, almost inaudible.

Right Apex Posteriorly. Nose open, inspiratory and expiratory sounds audible; nose closed, inspiratory vesicular sound clear, expiratory sound inaudible.

Left Apex Posteriorly. Nose open, inspiratory and expiratory vesicular sounds audible; nose closed, inspiratory vesicular sounds only are heard.

Over Middle of Chest. The characteristic normal vesicular sound is not present. Instead, one hears a rather rough interrupted vesicular type of breathing at some areas, while at others hardly any sound is heard.

At Base of Lungs. On the left side the sounds are better heard than on the right. By using Bowles' resonating stethoscope, when the nares were left open, I could detect both the inspiratory and expiratory sounds. With closure of the nostrils the inspiratory sound alone was audible.

Speech. These patients make attempts at speech by closing of the tracheotomy tube or fistula with their fingers, and during expiration set the vocal cords or remnants of the same into vibration. The resulting sound, which is a kind of a barking whisper, is transmitted by the osseous structures just as clearly as the normal spoken voice.

Case II.—This patient breathed freely through a large tracheal fistula, the tube having been discarded.

Cranium. At the occipital area cavernous breathing could be heard when the nares were open or closed. In the other case, when the nares and mouth were closed no sounds were audible; the column of air passing through the tracheotomy tube did not reach the nasal resonating chamber. In this case both the inspired and expired air had access to the nasal cavity, and sound was carried.

Acromion Areas. On the right side, when the fistula was closed, bronchial sounds were distinct; when the fistula was open, the sounds were very faint or imperceptible at times. The left side was the same.

Apices Right and Left. When fistula was closed, the respiratory sound was audible. The sound heard corresponded more to a weak and indistinct bronchial sound than a pure vesicular murmur. When the fistula was uncovered, the respiratory sound was very distant and its character doubtful.

Middle and Lower Lobes. The respiratory sounds were atypical. Bronchial breathing at the median line lacked the quality which characterizes it in the normal, and the vesicular murmur seemed to be replaced by a distant and weaker sound. At the bases posteriorly, inspiration was longer than expiration, and was louder, as the normal vesicular murmur should be. In the axillary aspect of the chest there was a short inspiratory sound and no expiratory sound was audible. Thus, the sounds over most of the chest seemed very distant and weak. Tactile fremitus was imperceptible. Vocal resonance could be heard.

The observations in these two cases show that elimination of the larynx does alter the auscultatory findings, but not sufficiently to change their character. They confirm the previous findings that the sound created within the nasal resonating cavity is a part of the "sound total" which presents itself to us for auscultation over the thorax.

Before my conclusion I wish to note that in this consideration I have dealt with the physiological only. It is needless to say that abnormal configurations and pathological conditions of any of the anatomical parts which enter into this sound-producing and sound-conducting system will respectively modify the findings.

By this study I intended leading up to the consideration of sound transmission in the various pathological conditions.

SUMMARY AND DEDUCTIONS.

In calling attention to the auscultatory findings at the specified areas of the thorax and skull, I desired first to set forth prominently, the sound-conducting ability of the osseous system, particularly the thorax. When it is fully appreciated that sounds emanating at one spot can be transmitted to another, the importance of studying auscultatory signs from such a viewpoint becomes apparent.

Thus, I found that the "bronchial breathing" heard at the acromial end of the clavicle has its origin at the manubrium sterni, which receives sound vibrations from the trachea behind. The cavernous breathing heard over the cranial bones, particularly the occipital, has its source of origin in the nasal fossa which acts as a resonator.

In the nasal fossa, the nasal resonator, a definite amount of sound is produced, and this sound added to the sound wave created along the lower portions of the respiratory tract, makes up the "sound total," which is heard when auscultating.

That the nasal resonator is an active factor in auscultatory sound production is readily appreciated by observing the weakening of the respiratory sounds which occurs when its action is eliminated. From this it is evident that auscultatory sound production does not begin at the larynx. This too, shows that the examiner must take into careful consideration the condition of the nasal resonator, and whether the mouth is open or closed, in the proper interpretation of his auscultatory findings.

The observations upon the tracheotomy cases throw light upon the part played by the larynx, which seems to be of less importance than is generally believed. They show that elimination of the larynx results in modification of the pitch and volume of the bronchial and vesicular sounds, but the essential characteristics of these sounds remain unchanged.

SOME GENERAL CONSIDERATIONS AS TO VISCERAL PTOSIS.

By A. L. Benedict, A.M., M.D.,

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A ptosis consists, essentially, in a gravitation of an organ, due to some weakness in its normal support. Originally applied mainly to the upper eyelid, and in Dunglison's dictionary of 1874 limited to various ocular conditions, ptosis in recent years has been discussed chiefly as a condition of certain abdominal viscera and, to a less degree, of the heart. While literally applicable to the pelvic generative organs, and properly so, other terms are more commonly employed.

The displacement of an organ outside of the body cavities, to employ a loose expression for an idea which it is difficult to express accurately, is not properly considered as a ptosis. Thus, one does not speak of a ptosis of the thyroid. Obviously, too, the dense, close-fitting walls of the cerebrospinal apparatus prevent the occurrence of this lesion for the corresponding organs.

As stated, ptosis implies a gravitational displacement. Thus, in the perpendicular posture, the displacement is downward and the direction is not necessarily nor, indeed, characteristically altered for other postures. Moreover, the downward displacement is liable to be chronic, and the support of adjoining viscera or of the body wall, more or less regularly for various organs, tends to prevent move-

ments in the horizontal plane, relative to the perpendicular posture of the body as a whole.

A displacement due essentially to encroachment, either of an enlarged organ or of some foreign growth or accumulation, as fluid, etc., or, on the other hand, to traction, as by cicatricial bands, is not essentially a ptosis, even if the displacement is downward, although it is not always practicable to discriminate with regard to the ultimate or complicating causes of displacements of this nature. The definition of ptosis as gravitational, that is, mainly downward in the ordinary vertical posture, must also be qualified to allow for the combination of other forces, as fixed points or planes of resistance, which deflect the organ from a strictly vertical displacement.

Disregarding the female pelvic organs, the conceivable ptoses are as follows: Cardioptosis, pneumoptosis, hepatoptosis, lienoptosis, nephroptosis, gastroptosis, enteroptosis (coloptosis), and more generally splanchnoptosis. The names are purposely given, as some writers substitute mongrel terms for some organs, and the collective ptosis is often designated visceroptosis. These terms cover all of the major organs of the thorax and abdomen. It is hardly conceivable that the suprarenal could be prolapsed without the kidney or the appendix without the cecum, at least.

It is extremely doubtful if the term pneumoptosis, or rather the corresponding conception, is tenable. The lung is a very light, distensible organ, necessarily conforming to the contour of the thoracic wall and floor, and any downward extension of the lung is due to a fault of the diaphragm or of subjacent structures, not to an essential prolapse of the lung itself.

The writer would insist that the term prolapse be limited to a dropping of an entire organ or, at least, of an anatomic unit, as a lobe of the liver or a considerable extent of the colon. Thus, a downward displacement of the heart, not essentially due to a fault of its supports, but to a dilatation, or other form of enlargement, is in no true sense a cardioptosis. This contention will probably not be disputed, indeed, it will more likely be regarded as a truism. It is made in order to support an analogous claim for the stomach. The term gastroptosis frequently occurs in medical literature. Nine times out of ten it applies to the inevitable sagging of the greater curvature of a dilated organ, or, at any rate, it is used without any demonstration that the stomach in its entirety is displaced downward. The term should not be used unless by *x*-ray examination, auscultatory percussion, or some allied method the upper portion of the stomach is also shown to be sagging from its proper level. However, it must be conceded that atonic gastric dilatation, that is, dilatation not due to pyloric obstruction, has many etiologic and pathogenic points in common with gastroptosis.

Hepatoptosis is, in the writer's experience, a very rare condition,

only two cases having been encountered in over a thousand physical examinations, and these in connection with other ptoses. A little consideration, however, will show that the condition is difficult to determine if one starts with the idea not to diagnosticate what cannot be actually demonstrated. In the case of a large liver, which is necessarily heavier than normal, a slight amount of sagging is inevitable and not to be considered a ptosis. Whether by deep ordinary percussion, auscultatory percussion and its modifications, x-ray examination, etc., the upper limit of the hepatic area extends higher than normal or not, it is very difficult to judge how much of the depression below the costal arch is enlargement and how much sagging. In the opposite condition, of contraction, the pull of gravity is diminished by the lessened mass of the liver, and the same puzzle, as to distinguishing between the size and relative position of the liver, is present. In actual ptosis the liver tends to rotate on a lateral axis, so as to give the impression of enlargement by physical examination. Then, too, neither with regard to shape, perpendicular diameter, nor relation to ribs, can we lay down exact normal standards for this organ. Finally, there may be mentioned the fact that there is a common tendency to find the liver enlarged or, at any rate, depressed below the costal arch when it is actually of normal size or even contracted. Even men of high standing often fail to realize that when they palpate the edge of the liver so many fingers' breadths below the costal arch, they must subtract the thickness of the abdominal wall which intervenes between their fingers and the liver. The liver may enlarge considerably by mere congestion. For example, the writer has seen the liver retract two inches during a half-hour operation on the gall-bladder, in which considerable blood was lost.

Barring extreme cases, it is doubtful if lienoptosis without enlargement can be diagnosticated. In most cases, the writer can make out by auscultatory percussion a small circular or elliptic area posteriorly, which apparently corresponds to the spleen, although great care must be exercised not to confuse the posterior projection of the gastric area with this. But the area varies so much in apparently normal subjects that it is practically impossible to draw conclusions as to ptosis or even to be absolutely sure that it indicates the spleen at all. The spleen, when considerably enlarged, is usually easily palpable below the ribs, but, as in the case of an enlarged liver, it is difficult to estimate the degree of true ptosis. Marked ptosis of the unenlarged or slightly enlarged spleen is a well-known though rare condition. The differential diagnosis from nephroptosis or other tumors is difficult.

The subject of nephroptosis would fill a volume. As the writer intends to discuss it more fully at a later date, only two points will be alluded to and these merely for the sake of eliciting information and criticism. It is commonly stated that manipulation of a kidney

will often, if not usually, produce albuminuria. This phenomenon the writer has never noted in a series of about 400 to 500 cases, though it should be admitted that a systematic examination of urine for a definite period after manipulation has not been made, nor has the kidney been purposely kneaded. Still, in most cases the urine has been examined within a day after palpation, and in many repeated examinations have been made. Secondly, no instance of a Dietl's crisis has been encountered in this series. In one case a physician reported such an instance, but on visiting the patient, absolutely no history of such an attack could be elicited.

(Uro) Cystoptosis can scarcely exist in the male, except in the sense of an extreme failure of development of bony and ligamentous structures or of the extension of the bladder into a ventral or other hernial sac. In the female partial ptosis is common as a cystocele.

There is no apriori reason why cholecystoptosis should not occur, although, as a matter of fact, the supports of this comparatively small and light organ are not often relaxed to any degree, even when it is weighed down by calculi, distention with bile, or growths. Moreover, at the best, it is not easy to palpate, and perhaps a true ptosis exists more often than it is recognized. It is scarcely necessary to state that the gall-bladder descends with a hepatoptosis.

The term enteroptosis is very commonly employed. Excepting with regard to the transverse colon, it is rather difficult to define this condition. The transverse colon is large enough and has a sufficiently definite location, so that it is usually possible, by a few examinations, to make out a coloptosis. However, there is an extreme and rather rare type of gastroptosis, which may be confused with ptosis of the transverse colon. This type of gastroptosis the writer has termed "banana stomach," from its shape and size. Various methods of intubation, auscultation of air blown through the tube, or of deglutition murmurs, of effervescence produced chemically, *x*-rays, etc., may be used to determine whether the area in question is the stomach.

It is theoretically possible to diagnosticate a typhloptosis by palpation of a low-lying, appendiceal root, perhaps, by vaginal touch, in addition to percussion, auscultation, *x*-rays, etc. Radiography might also be expected to enable the determination of ptosis of the colonic flexures. The sigmoid varies so very widely in length, shape, and position at necropsies that it is difficult to see how ptosis could be defined or diagnosticated with the body wall intact. Excepting in cases of stricture with enormous distention with gas and feces, the writer has not been able to diagnosticate any of these recondite conditions, and in such cases the applicability of the word ptosis is questionable.

Rectal prolapse is, in a sense, a ptosis, but the condition involves also inversion or even intussusception, and should, for practical

purposes, be kept in a separate category. So, too, hernias of all kinds, including diaphragmatic hernias, with descent of the thoracic organs, should be distinguished from true ptoses. In passing, it may be pointed out that neither a diaphragmatic hernia, unless of very rare type, nor the classic illustration of the tongue protruded from the mouth, is a true hernia, the essential definition of hernia including the presence of protruded enclosing membranes.

In a case of intestinal ulceration the surgeon very courteously gave the writer credit for diagnosticating a ptosis of the sigmoid or upper rectum by the use of a speculum. But it is quite beyond the writer's ability even to conceive how a ptosis could be diagnosticated by the use of an instrument which reposits, as it is introduced, and which allows the inspection of only a small circle of bowel at any one time.

By analogy, the more general term enteroptosis would indicate a ptosis of the small intestine. Ptosis of the duodenum, in whole or part, may often be surmised, or, by *x*-ray examination, actually demonstrated, in connection with gastroptosis and hepatoptosis. In one case the writer mapped out, both by *x*-ray and auscultatory percussion, what appeared to be an hour-glass stomach, but which proved to be a moderately dilated stomach, separated by a cancerous pylorus from a considerably dilated duodenum. The latter was somewhat prolapsed. Still, such a case does not answer fully the requirements of ptosis. So, too, as implied in the discussion of the colon, it might be possible to make out an abnormal position of the termination of the ileum. Between these extremes, what anatomy will tell us the normal location of the various sections of the small intestine, or what diagnostician can determine how far such locations are fulfilled?

A number of writers have described at length what they term enteroptosis. Their communications have been, in many instances, detailed and valuable, and, in a literal sense, there has been a sagging of the intestine generally, especially of the small intestine. But the condition that they have described has fulfilled none of the intrinsic requirements of the word ptosis, as established for other organs. There has been a hernial protrusion, a diastasis of the recti, a pot belly, a spinal lordosis, or a long trunk, perhaps with poor musculature. To include such conditions under the term enteroptosis reminds one of President Lincoln's answer to the question as to how long a man's legs should be: "I should say that they ought to be long enough to reach from his body down to the ground." The free intestine, that is to say, all the intestine not bound to the posterior wall of the abdomen, floats in its confines, on itself, in continually changing loops. It permeates all the abdominal cavity, and naturally extends as far as does this cavity, in any direction, either in a general or local protrusion. Unquestionably, thorough, routine postmortem or even operative investi-

gation of a large series might reveal ptoses of individual parts of the small intestine, but at present we have neither anatomic nor diagnostic bases for the use of the word enteroptosis.

Neither should the term enteroptosis be used, as it sometimes is, as a substitute for nephroptosis or a combined ptosis of several viscera. One might just as well say enteritis when he means nephritis or cholecystitis.

Except that the term is more non-committal, the same objection applies to the term splanchnoptosis. There is a general impression that a general splanchnoptosis is quite a common occurrence. Such a conception seems reasonable, and, as ptosis necessarily implies movability, barring secondary fixation, it is obvious that even a total splanchnoptosis would be diagnosticable and would not merely consist of normal relations of viscera at a lower level. The writer has never encountered an instance of total splanchnoptosis and very rarely one involving more than three organs. Extreme abdominal ptoses may occur independently of pelvic prolapses, and vice versa. While slender, neurotic, naturally small-waisted women offer the best material in which to seek for movable kidneys, and while the upright, ptotic stomach is also frequently encountered among them, there is no necessary occurrence of these ptoses, singly or associated. Similarly, broad, flabby, extremely multiparous women, with prolapsed pelvic organs, do not seem to be especially liable to ptoses of other organs, except that the intestine, of course, adapts itself to the pot belly and encroaches more than normally on the pelvic space. However, a word of caution is required in regard to these cases, as the transverse colon and stomach may really sag too low and still be high with reference to the umbilicus.

With regard to the skeletal deformities and muscular atony described as an important factor in "enteroptosis," it should be freely admitted not only that there is a sagging of the intestine following the contour of the abdomen, but that both the lack of anterior and inferior support and the general state of atonicity and malnutrition tend toward genuine ptoses. Still, it is surprising how often these ptoses are lacking.

For these reasons it seems best to discard the term "general splanchnoptosis" except for purposes of classification, and in each case to list the ptoses actually demonstrated.

MULTIPLE METASTATIC ABSCESSES OF THE HEART AND LUNGS IN PYEMIA.

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The very occasional occurrence of suppurative myocarditis or of circumscribed abscess formation in the cardiac muscle lends to either of these conditions sufficient interest to call for the report and description of each new case. Abscess of the heart is a condition that was known to the ancient physician. It is no more recognizable by clinical signs today than when it was studied on the Egyptian autopsy table. The symptoms and physical signs are those of toxemia, not of a definitely localized suppurative process, and not even of a definite cardiac clinical entity. Yet the possibility of such an occurrence and of such an involvement of the myocardium as was present in the instance described below should ever be borne in mind and have weight in determining both the diagnosis and prognosis in the given case of toxemia.

Beck and Stokes[1] have recently reported an instance of suppurative myocarditis as contrasted with the circumscribed abscess formation seen in cases similar to that here described.

The patient now reported was a trained nurse, aged twenty-four years, serving in the eye ward of the Philadelphia General Hospital. Her family history was entirely negative, both parents being alive and well and one sister a nervous invalid. The patient had never been robust, but was wiry, and always active and energetic. During childhood she had pneumonia; otherwise she had been free from severe illness. One year previous to the history here related she had suffered from a severe and extensive furunculosis, from which she had entirely recovered. Two weeks prior to the present illness, while on duty in the eye ward, a small pimple appeared on the right forehead above the eyebrow. Probably through fingering this pimple infection occurred, and on July 22, 1910, a severe cellulitis and carbuncular suppuration of the scalp followed within a few days. On July 24, 1910, she became quite ill, displayed a temperature of 101° F., and two days later 105° F., and complained of intense pain in the left side. She vomited rather than coughed considerable mucus, and had much nausea. On July 25 the pain seemed to distribute itself more generally throughout the chest, though the original agonizing pain persisted near the apex of the heart and the anterior axillary line. A culture from the scalp pus made by Dr. Randle C. Rosenberger yielded micrococci of suppuration. The right eye at this time became inflamed and discharged a thick pus from

[1] Jour. Amer. Med. Assoc., September 24, 1910.

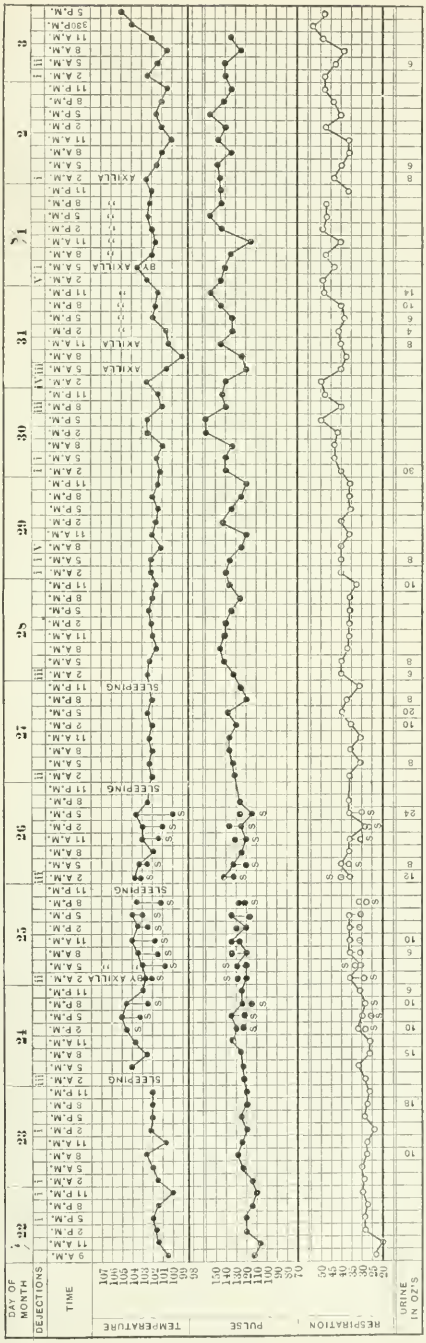

FIG. 1.—Temperature chart.

the conjunctival sac, which was examined for gonococci and other bacteria, with negative result.

When seen in consultation at the request of Dr. Frescoln, and later with Dr. William E. Hughes, the patient was decidedly toxic, though fully conscious, and in evident pain, which she indicated as most intense in the left side low down in the anterior axillary line. She related that three days previously she had a chill, and since then the pain in this location and sometimes throughout the chest had been constant and very severe. The right eye, the orbital tissues, and the eyelid on July 25 all appeared boggy, the temporal tissues were discolored and edematous, and the surrounding scalp suggestive of underyling infection.

The patient was of small frame, normal in contour. The skin was sallow, but not distinctly jaundiced. The whole of the right half of the scalp was involved in a cellulitis, which caused a dark bluish color of the tissues, through which numerous pustular openings discharged each about a drop of greenish-yellow pus. There were no other suppurative foci on the surface of the body. The cardiac rate was then 120 to 140, the respirations averaged 30 to 35, and there was much distress on breathing and coughing, mainly, as before, on the left side. There was also a small area in the left posterior chest near the angle of the scapula that, even to the lightest plapation, was exquisitely tender. Over the entire left lung a harsh friction was audible, heard loudest and evidently produced over the left scapular region. No rales were audible as yet over the left lung. Over the right lung the breath sounds were comparatively free, though over the right base posteriorly were heard a few tiny crackling rales.

On July 26 the patient experienced much distress from pain and labored breathing. On this day there also appeared a profuse urticarial eruption, whether as the result of small doses of quinine (1 grain three times daily) or of the toxemia did not appear clear at first, though on the withdrawal of the quinine the urticarial wheals gradually changed into hemorrhagic areas, some petechial others extensive in size. A few of the smaller petechiæ presented a tiny pustule in the centre. The patient also began to expectorate bloody mucopus and gave signs of widespread consolidation behind and below the left scapula. Loud, metallic, crackling rales became audible over the left axilla, and soon extended over the entire anterior lower lobe. The right eye and the surrounding tissues were more and more involved in a virulent suppurative inflammation, and pus extruded from dozens of small openings over the entire cranial surface.

On August 1 the pain and dyspnea were extreme; the patient was jaundiced and deeply toxic; the tongue dry and parched, and the abdomen greatly distended. Air hunger was intense. At this time there occurred a syncopal attack that caused the patient to appear

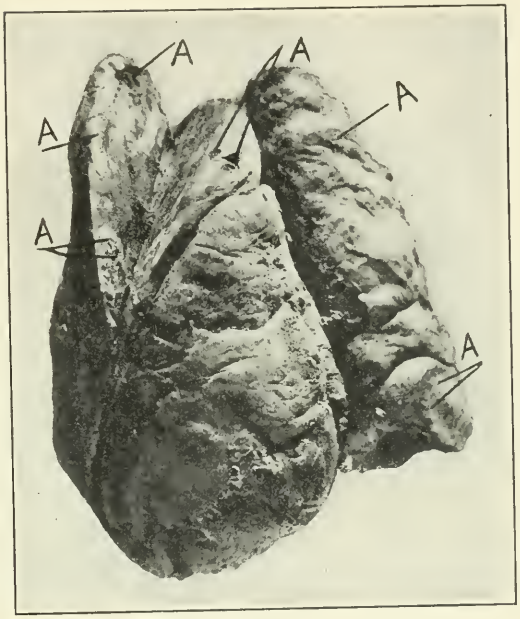

FIG. 2.—Lungs containing numerous abscesses (A).

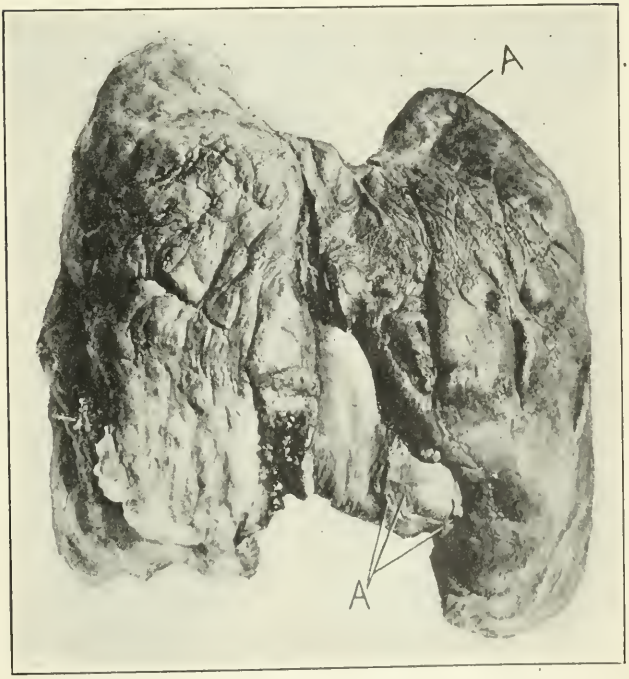

FIG. 3.—Heart, showing metastatic abscesses (A) near apex

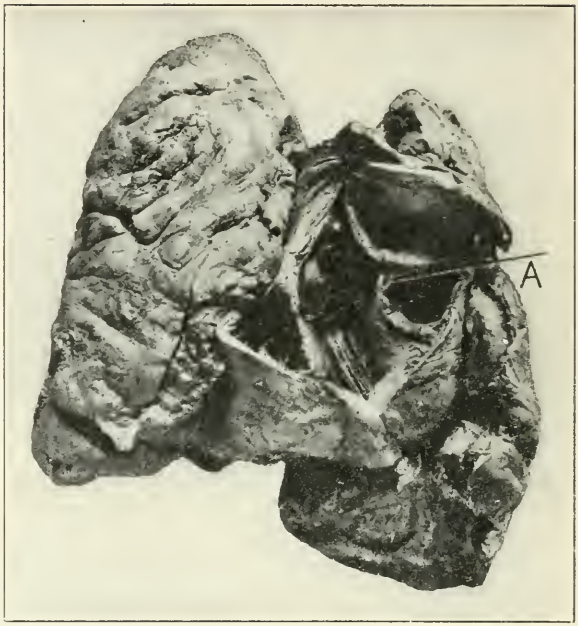

FIG. 4.—Heart, showing portion of large pus collection (A) in left ventricle wall.

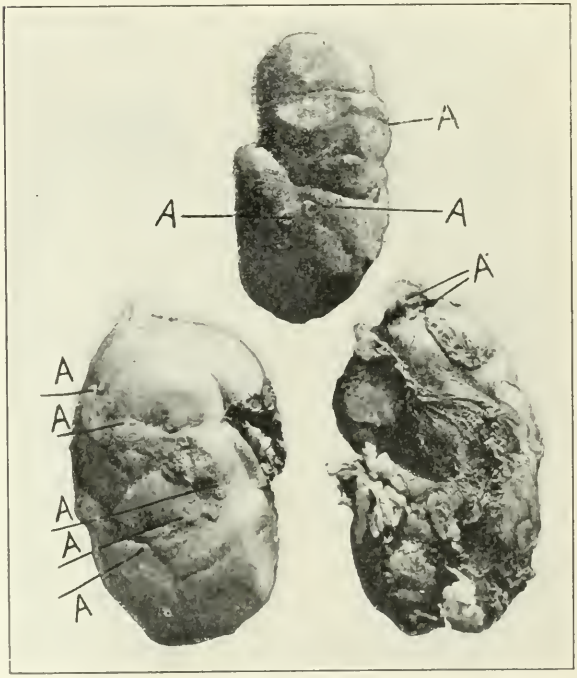

FIG. 5.—Kidneys, the seat of many small abscesses (A).

moribund. Free incisions had been made in the scalp early in the morning of this day by Dr. M. G. Warmuth, and a large quantity of thick greenish pus was evacuated through the incisions and through the myriad carbuncular openings. From the pus staphyloccocci only were obtained. An autogenous vaccine had been prepared from the micrococci obtained in the scalp pus earlier in the history of the case, and was used on this day, but without evident benefit. A pure culture of pneumococci was eventually obtained from the blood.

On August 3 the patient became even more deeply jaundiced, expectorated pure blood, and was evidently dying. Large metallic rales were heard over the entire left anterior chest (the patient was at this time too ill to examine needlessly). The next day she seemed for the moment stronger and more comfortable than at any time. The mind was again clear, the patient asked for food, said she was hungry, and took considerable interest in her surroundings. She again became toxic in appearance, however, and at 7 P.M. suddenly collapsed and died.

Autopsy Record. On August 5 section was made of the body, which had already been embalmed. The tissues were deeply bile-stained and of a deep saffron color, except the scalp, which was of a dark purple hue. Everywhere over the body were the petechial and ecchymotic areas noted during life. On opening the thorax the lungs were seen to be adherent at all points of contact with the pericardium. About one pint of seropurulent fluid was removed from each pleural cavity. Everywhere were also extensive adhesions binding the lungs to the thoracic wall. Both lungs were riddled with abscesses (see Fig. 2), the pus from which contained in every microscopic field a few pneumodiplococci. The heart was dilated, and the muscle, though hypertrophic, was flabby and weak. In the myocardial wall were multiple metastatic abscesses, several on the surface of the heart near the apex (see Fig. 3), and one large pus collection just below the anterior coronary opening in the left ventricular wall (see Fig. 4). Smears from the pus in the myocardial abscesses were examined, and in all were found great numbers of pneumodiplococci, as contrasted with the very few detected in the pus obtained from the pulmonary foci.

The kidneys also presented many small abscesses (see Fig. 5), both upon the surface and within the parenchyma. Two infarcts were found in each kidney. The spleen contained one small abscess beneath the capsule. The liver showed marked congestion and some fatty degeneration, but no localized pus foci. There was about one pint of clear serum in the abdominal cavity. The stomach, intestines, pancreas, and uterus and appendages all appeared normal.

AORTIC REGURGITATION.[1]

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It is not the object of this paper to present a complete study of the subject of aortic regurgitation, but simply to discuss some of the mechanical factors that come into play as a result of the lesion and contribute both to the physical signs and to the secondary changes in the heart itself. Occasionally it happens that valvular lesions are regarded too much from the mechanical standpoint, to the exclusion of other important conditions, but, on the other hand, they must not be overlooked, because the more perfectly we understand the different influences at work in each case the more probable is it that we shall be able to make life comfortable for the patient.

Factors Influencing the Momentum of the Regurgitant Stream. During diastole a stream of blood flows backward from the aorta into the ventricle with a momentum resulting from a number of factors, none of which are constant. (1) Gravity which must depend upon the position of the patient. (2) The recoil of the aorta, the walls of which have been stretched during systole, will naturally vary with the volume and force with which the ventricular contents have been propelled into the aorta, the condition of the aortic wall, and the degree of contraction in the peripheral vessels. (3) The ventricular suction at the commencement of diastole, which is only of momentary duration, and corresponds to the elastic recoil or relaxation of the myocardium rather than to active diastole, for at no time is the ventricular cavity a vacuum; nevertheless, this short negative pressure gives an initial impulse both to the auricular direct and aortic regurgitant streams. It is evident that in feeble cardiac contraction there will be little, if any, elastic recoil of the myocardium, and consequently this negative pressure may be entirely absent. (4) The effects of this stream will also be influenced by the area of the regurgitating column of blood, that is, by the size of the aperture of incompetence. All of these factors contribute toward the momentum of the regurgitating blood stream, and all of them are liable to vary from time to time in the same patient.

The Distribution of the Diastolic Murmur and Conditions Influencing It. This depends upon the direction of the regurgitant stream, which is modified by the nature of the valvular lesion and also by the force of the current; but both of these have to be considered in relation to the anatomical formation of different parts of the ven-

[1] Read before the San Francisco County Medical Society, March 14, 1911.

tricular walls, as well as in connection with the fact that the blending of the aortic regurgitant stream with that entering through the auriculoventricular orifice is liable to produce vibrations within the ventricle that are communicated to the cardiac wall, and thence to the chest wall and ear of the auscultator.

The diastolic murmur which accompanies this condition is recognized by most clinicians to be the most erratic of all cardiac murmurs in its area of distribution. The maximum intensity is most frequently not in the so-called aortic area, but over the *left* half of the sternum at the level of the third interspace or upper border of the fourth costal cartilage, or it may be over the right side of the sternum at the level of the third interspace, or at the apex and only at the apex. Furthermore, the distribution is not always the same from day to day in the same patient.

For more than twenty years, in consequence of experimental data, and also because of observation made in the postmortem room, an attempt has been made to infer from the direction in which the murmur is propagated which valve segment is affected, for it is very evident that the direction of the regurgitant stream must be influenced by its own force and by the position and character of the valvular aperture. Injuries of the left cusp tend to deflect the stream toward the septum, while those of the posterior cusp incline it in the direction of the apex, and those of the right cusp allow it to impinge upon the aortic segment of the mitral valve. This applies to perforations of the segments artificially produced, but pathologically the orifices permitting incompetence are generally between the margins of the segments, of irregular outline, with some parts of the valve more distorted than others, and in this way they are calculated to deflect the stream in an irregular manner, similar to that in which the direction and arrangement of a stream of water is changed when it passes through the battered orifice of a metal nozzle.

In cases of combined stenosis and incompetence the regurgitant stream must, in some instances, flow over vegetations projecting from the anterior portions of the cardiac surfaces of the aortic valves or from the wall of the aortic vestibule, and in this way modify the character of the murmur.

Again, variations in the area of distribution of the murmur in the same patient from day to day, apart from those cases of acute endocarditis, where the inflammatory process is continually changing, are probably due to variations in aortic pressure. If the left ventricle of a bullock's heart be opened without doing injury to the aortic valves, one of the segments perforated and water forced through it from the aorta by means of a pressure bottle, the direction of the stream will be modified by the pressure, because the water tends to flow through the orifice at right angles to the plane of the valve at that particular point. But as the surface of the valve is a

curvature, and as the valve contains elastic tissue, the relation of the aperture to other parts of the heart will vary with the degree to which the segment is stretched. This will be even more conspicuous in disease, for the margins of the valves are never identically injured in corresponding places, and according as the lunules are more or less distended, so will the coaptation of the three segments be modified, the shape and attitude of the incompetent orifice changed, and the direction of the blood stream correspondingly altered. Furthermore, the greater the force of the regurgitant stream, the longer does it persist in its original direction and the greater is its momentum within the ventricle, so that more powerful intraventricular vibrations are produced and conveyed to the cardiac wall.

But there are certain anatomical features of the cardiac walls that assist in conveying intracardiac vibrations to the chest wall. "The muscular portion of the wall of the left ventricle attains its minimum thickness at the apex, but the thinnest portion of the boundary is at the upper part of the septum, which consists entirely of fibrous tissue."[2] The septum extends from the right of the apex to the interval between the pulmonary and aortic orifices, that is, to a point behind the left half of the sternum at the level of the third costal cartilage.

It is peculiarly significant to notice how frequently murmurs of aortic incompetence have their area of maximum intensity at some point along this line, namely, an oblique line extending from the middle of the sternum at the level of the third costal cartilage to a point inside the apex, and it is still more suggestive when taken in conjunction with the fact that on the left side of the membranous portion of the septum is the vestibule of the aorta, because observation has shown that injury to the left aortic cusp tends to direct the regurgitant stream against this portion of the septum. It is, therefore, highly probable that in many cases of aortic incompetence the interventricular septum plays a prominent part in conveying intraventricular vibrations to different points on the chest wall and to the ear of the auscultator.

It is probable that there is still another factor in the production of the aortic murmur which will aid in explaining the vagaries of its distribution and quality. This sound is generally described as if it were produced at the aortic orifice alone and transmitted by the regurgitant stream impinging upon some point in the ventricular wall, but this by no means describes the true condition, because it depicts the ventricular cavity as an empty space into which the blood is pouring. The fact is that there never is a vacuum within the ventricle, but, on account of their elastic and contractile character, the walls are always in close contact with one another or with

[2] Cunningham's Anatomy, p. 791.

the blood contents; in other words, while the ventricular cavity varies in size with the degree of systole and diastole, nevertheless it is always full, even if the contents amount only to one or two drams of residual blood. The regurgitant stream, therefore, pours back into a cavity that is already full and is undergoing further diastole by the blood entering through the mitral orifice, and these two streams meet at some point which will vary with the angle of entrance of that coming from the aorta, their intersection resulting in the production of numerous eddies which may be audible, but which are at least capable of causing vibration in whatever tissues are nearest to the storm centre of the eddy, so to speak. It may be in the mitral valves, or the chordæ tendineæ, or the papillary muscles, and consequently, the line of transmission varies with the particular group of muscular fibers that are connected with the tissues thus agitated.

We are apt to forget or doubt that vibrations produced inside the heart can throw the cardiac walls into vibration, but we must remember that the interventricular septum, the papillary muscles, and the chordæ tendineæ are not outgrowths of some fibrous substance from the inner surface of the heart, but are rearrangements of the myocardial fibers without any interruption in their continuity. Consequently, vibrations produced in these intraventricular projections may be carried along the fibers to their place in the cardiac wall and through the thoracic parietes to the ear of the auscultator.

These intracardiac fibers are represented in different parts of the ventricular walls; some of the parietal fibers from the front and left side enter the base of the posterior papillary muscles, while those from the back and right side terminate in the anterior papillary muscle. "The muscular fasciculi which enter the papillary muscle are continued, by means of the chordæ tendineæ, to the flaps of the mitral valve and so to the fibrous ring around the mitral orifice."[3] It is quite possible that this identity of intraventricular with parietal fibers is largely responsible for the variations in areas of maximum intensity of cardiac thrills and murmurs.

Among other matters of interest in the study of cases of aortic regurgitation are the changes that take place in the left ventricle and auricle. These are frequently discussed as if the enlargement of the ventricle were due to pressure from the volume and force of the aortic regurgitant stream, and the auricular increase were the result of a compensatory effort consequent upon failure of the left ventricle. But for the following reasons it is probable that the changes in the left auricle and ventricle take place simultaneously and that the left auricle is responsible to a very great extent for the dilatation of the left ventricle.

The increased capacity of the left ventricle is the result of a

[3] Cunningham's Anatomy

forcible dilatation, owing to the regurgitant stream entering under pressure at a time when the ventricular walls are relaxed and the blood is simultaneously pouring forward through the auriculoventricular orifice, so that when the auricular systole is due, it finds that it has to discharge its contents into a ventricle which is already better filled than it should be at this period of the cardiac cycle. Consequently, the ventricle must dilate that it may accommodate the additional quantity of blood, or the auricle itself must yield under the strain. Fortunately, the reserve capacity and power of the left ventricle is considerable, so that in very many cases its elasticity permits an increased capacity without the infliction of any injury to the muscle fibers, and the reserve force is sufficiently great to discharge the increased volume of blood into the aorta with each systole, and thereby maintain compensation. In accordance with physiological laws, the cardiac muscle should hypertrophy in response to this increased amount of work, but this process, which is a gradual one compared to that of dilatation, will take place only if the coronary circulation is adequate to supply the demands for increased nutrition, and if the patient's habits are so regulated that he lives well within the working capacity of his heart and allows time for additional muscular growth before attempting any exertion. In cases of the cardiac variety, occurring in young people, it not infrequently happens that perfect compensatory hypertrophy takes place, the increased capacity being sufficiently great to accommodate the additional quantity of blood, and the hypertrophy strong enough to discharge it into the aorta. Such compensation, however, demands (1) that the coronary arteries shall be healthy, hence it is nearly always impossible in the arteriosclerotic variety; (2) that the amount of regurgitation shall be small, because a large amount of regurgitation must quickly lower the aortic pressure and thus interfere with the proper filling of the coronary vessels; (3) that the heart shall not be subjected to any strain while the compensatory hypertrophy is developing. It must not be forgotten that the left auricle participates in producing and maintaining compensation even at this time.

The changes in the left auricle take place simultaneously with those in the ventricle, and are not secondary to ventricular failure. There is too much tendency to attribute the dilatation of the left ventricle to the regurgitating stream alone, but the fact remains that the auricular contraction which completes the ventricular diastole must contribute a very large quota of the distending power; because, no matter how full the left ventricle is of regurgitated blood, the auricle attempts to force its contents forward, and thus, through the auriculoventricular orifice, exercises a pressure which, according to Pascal's hydrostatic law, must be equal in all directions and, therefore, prove to be a powerful factor in stretching the ventricular walls. The left auricle, therefore, from the very first, has

a tendency to hypertrophy in accordance with the physiological law that muscles hypertrophy under increased work, but, of course, the degree of hypertrophy will vary with the amount of work imposed and the capacity for increased nutrition.

It appears to me, from such considerations, that it is a mistake to regard the auricular changes as a result of failure of ventricular compensation, the auricle and the ventricle must suffer together, and when the latter begins to fail from lack of adequate coronary circulation, so will the former. If we accept the idea, so frequently expressed, that auricular hypertrophy does not begin until failing compensation has permitted muscular mitral incompetence, then we must ignore the fact that in cases of aortic regurgitation, the auricle is working against increased resistance, and we must believe the improbability that the same coronary circulation which is inadequate to maintain an established ventricular hypertrophy, is quite capable of producing an auricular hypertrophy. Unfortunately, morbid anatomical statistics are not of much value in enabling us to arrive at a conclusion upon this subject, for while they show that in the majority of instances both auricle and ventricle have undergone changes, on the other hand, those cases have generally reached the stage of muscular failure before death took place, and consequently do not indicate when the process began. Clinical evidence is not wanting to demonstrate that in aortic disease there is an increased intraventricular pressure that extends backward beyond the mitral valve to the auricle and even into the pulmonary system. Hemoptysis, in cardiac valvular disease, is general accepted as a symptom of high pulmonary pressure. Some years ago, at Guy's Hospital, London, statistics were collected from all cases of hemoptysis occurring in valvular disease, with the object of ascertaining the valve lesion in which pulmonary hemorrhage was most common. It was found that 59 per cent. of the cases were, as might have been expected, examples of mitral stenosis, a smaller number presented single or double lesions of the aortic valves, while uncomplicated mitral incompetence furnished fewer examples of hemoptysis than any other valve lesion.

Many years ago Balfour called attention to the influence that the regurgitant stream, operating under Pascal's law, would have in producing ventricular dilatation, but he omitted to mention the much greater results that must be obtained from the left auricle working on the same principle. When we reflect that the capacity of the normal auricle is almost as great as that of the ventricle, and that Pascal's law, which maintains that pressure applied anywhere to a body of confined liquid is transmitted by the liquid so as to act with undiminished force on every square centimeter of the containing vessel, is the principle upon which such powerful apparatus as the hydraulic press and hydraulic elevator are constructed, we can realize what an enormous pressure the auricle exerts upon

the inner walls of the ventricle when it contracts upon that cavity already full of blood.

Arguing from such premises, it would seem reasonable to conclude that compensation for any degree of aortic incompetence from its very commencement depends upon the capacity of the left auricle and ventricle to undergo hypertrophy. But compensation may never take place either because the amount of regurgitation is beyond the combined powers of auricle and ventricle from the very commencement, or the patient is not kept at rest for a sufficient length of time to permit the growth of the necessary muscular tissues, or the condition of the myocardium and coronary vessels may be such as to make hypertrophy impossible. This is especially the case in the arterial variety of aortic incompetence, as this pathological lesion is very liable to be associated with atheroma of the coronary arteries or some other degenerative changes.

It must be borne in mind that in almost every instance, even when the most satisfactory compensation exists, it is only a matter of time until failure will occur, and one cannot help being impressed with the rapidity with which failure progresses when the downward process has once commenced; yet the reason is not far to seek. The continual increase of muscular tissue ultimately puts the myocardium beyond the nutritive power of the coronary vessels, especially in the arterial variety of incompetence. Even in the majority of endocarditic cases the coronary vessels have been taxed to their fullest capacity, and, as the degenerative changes consequent upon the increasing years of the patient are superadded to the original lesion, it is natural that failure should take place rapidly.

As the great majority of cases of aortic incompetence are combined with aortic stenosis, we can readily understand that the dilatation will be still greater; in fact, any disease of the aortic orifice that tends to increase the amount of residual blood in the left ventricle to such an extent as to increase its capacity and offer abnormal resistance to the influx of blood from the auricle must, under Pascal's law, increase to a very great extent the strain upon the ventricular wall during auricular systole. This strain may be within the capacity of the elasticity of the muscular fibers, and under such conditions no harm may result, but if it exceeds this point the lesion must terminate sooner or later in failure of compensation.

Stewart[4] produced aortic insufficiency in dogs by means of MacCallum's valvulotome, and after the operation the animals were kept in a separate room with a yard attached and allowed to run about it at will. The hearts were examined at periods, varying from four days to three months. He obtained a standard by examining twenty dogs and determining the proportion of the total heart weight in each to its body weight, and then the proportional

[4] Jour. Exper. Med., February, 1911.

weight of each left ventricle, right ventricle, septum, and the combined auricles to the body weight, and found that after operation, on making an average of the weights, the heart was approximately one-third larger than normal. The average increase showed 40 per cent. for the total heart, 59.3 per cent. for the left ventricle, 33.7 per cent. for the septum, 10.7 per cent. for the right ventricle, and 50 per cent. for the combined auricles.

Dr. Stewart believes that hypertrophy of the heart is due to increased work; that in the left ventricle the stimulus resulting in increased force of contraction lies in the greater tension applied to the ventricular wall during diastole, the hypertrophy of the septum is simply a hypertrophy of the fibers of the left ventricle that pass through the septum, and the hypertrophy of the right ventricle is confined to the muscular fibers that are common to both ventricles.

It will be noticed that in all cases the auricles were found to be hypertrophied as well as the ventricles, even in the earliest cases, and it is this simultaneous change in auricle and ventricle that has been contended for in an early part of this paper. He does not attribute this auricular hypertrophy to increased resistance to auricular systole, because he did not find "evidence of increased distention such as could be caused by an increased auricular pressure," but he noticed that when the left ventricle was incited to increased contraction there was a sympathetic increase in the force of the auricular contractions. No explanation of this sympathetic action can be given at the present time, but there is strong presumptive evidence of the "existence of an intracardiac reflex which maintains a coördination in the force of the systolic contraction between the chambers of the heart." The observations by Stewart do not in any way invalidate the contention that auricular contraction plays a prominent part in dilating the left ventricle because it is not necessary that an increased amount of blood should be propelled through the mitral orifice, the dilating power lying in the additional amount of blood in the left ventricle, as a result of aortic regurgitation, while the force of the auricular systole remains constant or is increased, as stated by Stewart.

More experiments showed another matter of special interest in regard to treatment, namely, "the remarkable rapidity with which the heart hypertrophies after the production of aortic insufficiency. This hypertrophy is well established after one week, and at the end of five days there is sufficient evidence to show that even the enlargement is in progress." We must remember that Stewart was working with normal heart muscles, and that clinically, where one is so frequently dealing with a co-existence of aortic incompetence and myocarditis, the extent of injury to the left ventricle must vary, but this does not in the least invalidate his conclusions.

Such considerations should not be regarded simply as medical

sophistries of no practical importance; on the contrary, they explain many clinical points and afford the indications for treatment. A thorough appreciation of the manner in which compensation is established and maintained, together with a recognition of the difficulty of restoring compensation when it has been lost, can only be obtained from a perfect knowledge of the cardiac mechanism and the manner in which it is liable to suffer under various abnormal conditions.

It is a fact that in many instances aortic lesions are regarded too lightly at their inception, and a patient allowed to resume active duties before there has been time for sufficient compensatory hypertrophy to develop, with the result that the mitral orifice becomes incompetent, and this is much harder to overcome when associated with an aortic lesion than when it occurs alone. Clinicians will generally admit this to be the case, and it is not difficult to find the explanation. Cases of muscular mitral incompetence can be relieved only by resting the heart and improving its nutrition, and success in the latter direction depends upon the possibility of restoring and maintaining an adequate circulation through the myocardium itself. To attain this end a rise in aortic pressure must be obtained, because this is one of the chief factors in determining the flow of blood through the coronary arteries; but the constricted aortic orifice, by diminishing the volume of blood entering the aorta or the incompetent valves which allow the blood to escape, present obstacles to the production and maintenance of normal aortic blood pressure which do not exist in the uncomplicated mitral lesion.

RECENT ADVANCES IN ANATOMY AND PATHOLOGY OF THE HEART FROM A CLINICAL POINT OF VIEW.[1]

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In a period of transition, such as that which at present involves our knowledge about heart disease, it is difficult to appraise properly what is and what is not important. To sum up the change in viewpoint which the subject is undergoing, it may be said that while up to five or six years ago we concerned ourselves with valvular lesions, and devoted all our energies to diagnosticating them from the point of view of sound and murmurs, and to a less extent from that of dilatation, as evidenced by percussion, palpation, and transillumination, now we have come to regard the heart as a whole, and to

[1]Read before the New York Academy of Medicine, April 20, 1911.

lay more stress on its working muscular portions and less on its automatically acting valves. It is not meant that valvular defects, either acute or chronic, have assumed a subsidiary place in our study, but that muscle function as such has been raised to a position of such importance that phenomena, which formerly were unrecognized clinically, are now capable of furnishing us with much valuable information both from a diagnostic, prognostic, and also, as many are hoping, from a therapeutic viewpoint. If we dismiss valvular diseases, therefore, from this survey, it is not because we consider them unimportant, but because recent advances have not been in their direction.

About thirty years ago Englemann and Gaskell, by extensive experiment, first placed our views about the functions of the heart muscle on a more exact basis. As a result of their work we have now come to speak of the heart muscle as possessing the functions of irritability, contractility, rhythmicity, and conductivity (in Engleman's phraseology, the bathmotropic, inotropic, chronotropic, and dromotropic functions of the heart muscle). We do best when we investigate heart muscle and heart disease under these separate heads, since frequently one patient suffers from a defect of only one of these functions, while another suffers from a combination of two or more, either as the ultimate result of a valvular lesion or, what is coming to be recognized as almost as common, a functional disturbance without the existence of a valvular defect. From a clinical point of view much has been added to our knowledge of rhythmicity and conductivity, but scarcely anything to that of irritability or contractility. As I shall point out, even that function of which we know most, namely, conductivity, leaves many points quite unexplained.

When we investigate the anatomical facts which underlie these functions of heart muscle, we are obliged to subdivide them into those which are muscular and those which are nervous, and to assign to each its proper domain.

The teaching that nerve fibrils surround and themselves interlace about the muscle fibers of the main body of the ventricular musculature is already old and accepted. Much has been added to our knowledge of the location of ganglia within the heart both of man and the lower animals. More recently, Tawara,[2] Wilson,[3] Engel,[4] and others have demonstrated the presence of nerve fibrils in the same sense about the auriculoventricular bundle, described by Kent,[5] His,[6] Braeunig,[7] Retzer,[8] Humblet,[9] Tawara,[10] and in

[2] Das Reitzleitungs system des Säugetierherzens, G. Fischer, Jena, 1906.
[3] Proc. Roy. Soc., 1909, Series B, vol. lxxxi, pp. 151 to 164.
[4] Ziegler's Beiträge, 1910, Band xlviii, 499 to 526.
[5] Jour. of Physiol., 1893, xiv, 233 to 254.
[6] Arbeit. aus der med. Klinik zu Leipzig, Leipzig, 1893, 14 to 50.
[7] Arch. f Anat. u. Physiol., Anat. Abt., 1904.
[8] Ibid.
[9] Arch. Intern. de Physiol., 1904, i, 278 to 286.
[10] Loc. cit.

some species have even shown that ganglion cells can be found far down in the ventricle in close union with the ventricular branches. These anatomical facts are known, but as yet nothing has been added to our knowledge of their function, and, more especially, no clinical abnormality has been correlated with a defect or lesion involving them. Furthermore, although a considerable literature has been accumulated in relation to the extrinsic nerves and central ganglia, both anatomical and physiological, it must be confessed that, in spite of the many facts collected in regard to the action of the vagi, the accelerators, and the depressor nerves, clinical knowledge of them is very deficient, and in many respects absent. Finally, it may be pointed out that there exists practically no investigation which relates the paths and distribution of the extrinsic with the system of intrinsic cardiac nerves.

The most that can be said is that certain manipulations of the extrinsic nerves produce certain effects and that the calling forth of these effects are very limited in number and are not constant phenomena. Here then is a large though difficult field for future investigation, and it would seem that, until much more knowledge along these lines is at hand, a myogenic and a neurogenic doctrine may be useful as points of view from which to investigate, but these doctrines should certainly not furnish a basis for the erection of hostile camps, from both of which polemics constantly keep pouring forth.

The study of the muscular architecture of the heart has brought us a large body of facts which have proved clinically extremely useful, even though this study has been concerned only with the functions of conduction and rhythm. Great advance was made after Gaskell and Englemann gave utterance to the doctrine that the propagation of an impulse once formed was conducted to other and appropriate locations in the heart by means of the heart muscle, and that in the muscle as such resided this function of conduction. Unfortunately no muscular connection between auricles and ventricles was known in the eighties, and it was not until 1893 that anatomical confirmation was given this theory by Kent[11] and His, Jr.,[12] who found what is now recognized as the auriculoventricular bundle. Braeunig,[13] Retzer,[14] and Humblet[15] confirmed the existence of this structure, but it remained for Aschoff and Tawara[16] to find its beginning in the lower interauricular septum and its ending at the venous base of the heart, in the papillary muscles. At the beginning of this conduction system and where the auricles join it, Tawara described a structure which is now called by his name, the node of Tawara, quite different in its anatomy from the rest of the heart muscle.

[11] Loc. cit. [12] Loc. cit. [13] Loc. cit.
[14] Loc. cit. [15] Loc. cit. [16] Loc. cit.

A point which should be clearly made is that no part of this A-V system should be called embryonic or an embryonic remains. Whoever has examined embryo hearts will know that it has no similarity with embryonal cardiac muscle. And Keith[17] has said: "If by embryonic is meant that they resemble the cardiac fibers of the heart of the embryo, then nothing could be further from the truth; if by embryonic is meant the fact that only the superficial stratum of the fibers is striated, the interior being undifferentiated cell substance, then in this feature they are embryonic. They are cardiac fibers which have specialized in a peculiar direction; their fibrillar structure is especially distinct."

To return, however, to the node of Tawara. Much has been written about its function, both as a pacemaker for the heart in abnormal conditions, a function once ascribed to it by Mackenzie, but now entirely abandoned by him, and as a site for the formation of so called atrioventricular extrasystoles. Actually there is known to us only one series of experiments which has been able to ascribe a definite function to this structure, and this is contained in a paper by H. E. Hering,[18] in which he maintains that the node of Tawara delays conduction. He ascertained this fact by stimulating below the level of the node and calculating the conduction time from the instant of stimulation until there occurred contractions of the auricle on the one hand and the ventricle on the other, and from these making the necessary deductions. Further than this nothing is known about the node. Aside from the node and bundle, the demonstration of nerve trunks, nerve fibers, and nerve ganglia in the conduction system, and a demonstration of the constant union of the A-V node with the auricles—a point that was necessary to complete the knowledge of the anatomical path and to show that normal automatism was a function which need not be ascribed to the auricle any more than to the ventricle—complete our anatomical knowledge about the auriculoventricular conduction system.

Knowledge about rhythmicity was augmented by the description of a node similar in structure to Tawara's in the wall of the right auricle, by Keith and Flack.[19] It begins at the junction of the superior vena cava and the upper border of the right auricular appendix and extends from there downward a varying distance in the direction of the sulcus terminalis. Structures similar to this are found at other sites, and may ultimately be shown to have functions not now ascribed to them, but we will at this time neglect them. The sino-auricular node has communications with auricular musculature in every direction. Its site and microscopic anatomy have

[17] Lancet, 1906, ii, 359 to 364.
[18] Pflüger's Arch., 1910, cxxxi, 572 to 581.
[19] Jour. Anat. and Physiol., 1907, xli, 172 to 189.

been confirmed by Koch[20] and other observers. That rhythmicity—stimulus production—has its seat in this node and that it acts under normal conditions as the pacemaker of the heart, was a function originally claimed for it by Keith. That this function resided in this region had been presumed by McWilliam,[21] Adam,[22] Langendorff and Lehmann,[23] Erlanger,[24] and Hering.[25] Since then, except only the negative experiments of Jaeger[26] and Magnus-Alsleben,[27] investigations by Lewis,[28] Lewis and Oppenheimer,[29] Wybauw,[30] Cohn and Kessel,[31] have tended to support and confirm this view.

I have said that the sino-auricular node communicates at its entire circumference with the auricular muscle. Thorel[32] imagined, however, that a communication between it and the A-V node was necessary for physiological reasons. The assumption was not, however, required by what is known of muscular conduction, and was not borne out by many other observers who failed to substantiate his anatomical findings. From the point of view of anatomy, therefore, counting more especially from the time of Braeunig and Retzer, the last seven years have put us in possession of the sino-auricular node, described by Keith and Flack, in which most probably resides the pacemaking function of the heart; and of the auriculoventricular system, through which stimuli pass from the auricles to the ventricles, so maintaining correlated contraction between these two pairs of cavities.

When we turn to that portion of the pathological anatomy of the heart which deals with the four divisions of its function above named, we find again, and naturally, that investigation has been confined only to the functions of rhythmicity and conductivity. It may be that the other functions have no anatomical substratum, and it may also be that all the functional deficiencies in these two, that is, rhythmicity and conductivity, cannot be explained anatomically, but the fact remains that anatomical explanations are at hand only for these two.

Sixty per cent. of all cases of irregularity of the heart fall under the heading of the so-called pulsus irregularis perpetuus, known also as the completely irregular pulse, nodal rhythm, and indeed by a variety of other names.

[20] Deutsch. med. Woch., 1909, No. 10, pp. 429 to 432.
[21] Jour. of Physiol., 1888, ix, 167.
[22] Pflüger's Arch., 1906, Band cxi, 607 to 619.
[23] Ibid., Band cxii, 352 to 360.
[24] Amer. Jour. of Physiol., 1907, xix, 125 to 174.
[25] Pflüger's Arch., 1907, cxvi, 143 to 158; Münch. med. Woch., 1909, lvi, 845.
[26] Deutsch. Arch. f. klin. Med., 1910, Band c, 1 to 11.
[27] Arch. f. exp. Path. u. Pharmak., 1911, lxiv, 228 to 243.
[28] Heart, 1910, ii, 23 to 47.
[29] Ibid., 147 to 169.
[30] Arch. de Physiol., x, i. Quoted from Münch. med. Woch., 1911, No. 4, p. 215.
[31] Arch. Intern. Med., 1911, vii, 226 to 230.
[32] Münch. med Woch., 1909, No. 42, p. 2159.

The history of its explanation is an interesting example of the history of anatomical and physiological advance. When Mackenzie[33] first described the condition, he believed it to be due to auricular dilatation and paralysis. At that time the anatomy of the A-V system was practically unknown. But paralysis meant atrophy, and Mackenzie soon saw that cases with a pulsus irregularis perpetuus might actually show hypertrophy of the right auricle. Then it happened that the A-V node, supposed to be embryonal in structure and therefore of pacemaking fiber, was credited with the function of stimulus production. Lying between auricles and ventricles, and almost equidistant between them, impulses starting here and going in both directions would arrive at and set in motion both pairs of cavities at the same time. The explanation was simple; it accounted for the auricular hypertrophy, for the auricle kept beating; it accounted for the absence of the A-wave in the jugular pulse, since auricles and ventricles would be beating synchronously; it even accounted for the increased auricular rate often found. At the same time, to lend weight to the theory, Keith found a variety of lesions in and about the A-V node and bundle; these formed the factors which were alleged to irritate the A-V node to increase its activity.

The explanation neglected, however, the doctrine that automatically beating heart portions beat regularly and not irregularly, and herein lay the weakness of the explanation, a weakness that had been pointed out as an *a priori* objection. The explanation was, however, held until the fall of 1909, when Lewis,[34] and Rothberger and Winterberg[35] were able to demonstrate conclusively that the irregularity was due to auricular fibrillation, a theory which explains auricular hypertrophy, an absent A-wave from the jugular pulse, and by comparing the experimental with the clinical tracings, the perpetual irregularity as well.

Now the anatomical interest shifted from the A-V system to a study of the right auricle. Schönberg,[36] Hedinger,[37] Koch,[38] have reported histological studies in this region, while many others are still in progress. The first studies of Schönberg and Hedinger may be briefly dismissed; they concerned themselves with lymphatic infiltration in a strand of auricular muscle which ran from behind and below, upward and forward on the superior vena cava. Wenckebach has supposed that if stimuli were produced at the entrance of the great vein to the auricle, over this pathway the stimuli must be conducted to the auricle. This notion is, of course, no longer held, and therefore lesions in this area no longer deserve the

[33] Brit. Med. Jour., 1904, i, 529.
[34] Heart, 1910, i, 306 to 372.
[35] Pflüger's Arch., 1910, Band cxxxi, 387 to 407.
[36] Frankfürter Zeitschr. f. Path., 1908, ii, 153 to 180; ibid., 462 to 485.
[37] Ibid., 1910, v, 296 to 322.
[38] Berl. klin. Woch., 1910, 1108 to 1112.

attention they once received, nor have they the significance once attached to them. In the sino-auricular node, however, Koch and others have found subendocardial fatty infiltration, small hemorrhages, subacute inflammatory changes, injuries to the nerves and ganglia by connective-tissue growth, occasional lesions in the afferent vessels, and more or less diffuse connective-tissue proliferation. These lesions cause destruction of the structures of the sino-auricular node. Such lesions, not by any means uniform, nor all found in any one heart, are designated as lesions sufficient to injure the pacemaking function of the node and so induce either fibrillation directly, or, in any event, to remove the controlling influence of the sinus, in such a fashion as indirectly to permit fibrillation to ensue. As I shall point out later, in speaking of the lesions of the A-V system, enough cases have not yet been examined nor sufficiently examined to make it advisable to correlate definitely anatomical lesions with functional change; in short, to make the anatomical changes sufficient explanation for the onset of fibrillation. Furthermore, it must be borne in mind that perpetual irregularities are of varying rates, now slow, now fast, and that there are cases in which the rate changes several times during the progress of the case. Therefore, while these anatomical advances and findings are valuable, interesting, and possibly final, enough is not known to consider them conclusive, and harm rather than good may be done by accepting them now.

I turn now to what is known of lesions of the auriculoventricular system and their clinical manifestations. So far isolated lesions involving either the auriculonodal junction or the auriculoventricular node itself are not known. Lesions have been described here, such as subacute, acute, and gummatous inflammations, but these are correlated with no clinical manifestations and require no further notice. When we go on to the main stem, however, a variety of lesions are noted. These may be divided into those which form complete transverse lesions of the bundle, in the same sense that there are complete transverse lesions of the spinal cord, and incomplete transverse lesions. This latter group contains both disseminated lesions and lesions which do not completely divide the bundle.

In the group of complete transverse lesions are enumerated tumors, both benign and malignant, metastases or infiltrations; inflammations, usually syphilitic, among which the calcified gumma plays an important part; and degeneration due to vascular disturbance, either thrombotic or embolic, or endarteritic. These complete lesions, so far as I know, all cause complete auriculoventricular dissociation, and may or may not be associated with the Adams-Stokes syndrome.

In the second group are those cases in which the lesion does not divide the A-V bundle completely. In these there are found the products of chronic inflammation, firm old connective-tissue

infiltration of the main stem, and infiltrations with rather large quantities of fat tissue. A special type consists of the presence in the bundle of large blood sinuses which have materially reduced the diameter of the bundle. It must be confessed that in the group of incomplete transverse lesion, cases are found where the auriculoventricular dissociation is complete, and others where it is partial. Whether the amount of injury alone is responsible for the varying degree of block or whether additional factors related to nerve control, nerve destruction, or nerve tone, are here involved, more expecially in the cases of complete dissociation, cannot now be properly appraised.

A third group[39] of cases must be added in which there are marked lesions of the bundle, but in which, clinically, all types of heartblock are demonstrated, from lengthened A-C intervals to complete dissociation, changing from one form to another in rather a startling fashion. To account for such cases, it has been supposed that the block has been from time to time increased and then diminished by the presence of inflammatory processes which undergo exacerbations and then subside, and which in their organization tend effectually ultimately to destroy the bundle.

In addition to these three groups is a fourth, in which heart block has existed clinically for years, as in Krumbhaar's[40] case, in which a lesion commensurate with the clinical findings cannot be demonstrated. In fact, it can be shown that the hearts in such cases contain lesions less in amount than are observed in hearts known to present no manifestation of disturbed conductivity during life.

Finally, there are a few cases in a fifth group in which, through inflammation or otherwise, one or other of the ventricular branches of the A-V system have been found cut off from the main stem. These cases reported by Eppinger,[41] aside from rather vague but certainly distinct clinical manifestations, have been diagnosticated electrically, and are of great clinical interest.

We have now summed up lesions in the heart involving the sino-auricular node and having their expression possibly in the cases of perpetual irregularity. We have also shown what lesions occur in the auriculoventricular system, and have shown their relation to heart block. We have not considered a number of the other irregularities, also chronotropic functions, expressed in extrasystoles and in praoxysmal tachycardia.

Whether chronic and acute interstitial myocarditis plays a role in the production more especially of ventricular extrasystoles is not known. The assumption is held, nevertheless, and the cases are called cases of cardiosclerosis. It is, however, a fact that there is no definite correlation known as yet between abnormal structure

[39] Quart. Jour. Med., 1910, iii, 126 to 152.
[40] Arch. Int. Med., 1910, v, 583 to 596.
[41] Zeitschr. f. klin. Med., 1910, Band lxxi, 157 to 164.

and abnormal function in any of these cases, nor are the limits of structural change in general convertible into the extent of functional deficiency. An attempt in this direction has been made by Moncke-berg[42] when he considered certain cases of sudden death due to fatty degeneration of the A-V bundle, but his findings have been both confirmed and denied by Engel,[43] and their status is not secure.

Aside from the functions mentioned, little is known. Much is left to be investigated, notably in the domain of irritability and of contractility of heart muscle, expecially in acute infections and in chronic degeneration. The string galvanometer, which produces electrocardiograms, at first seemed destined to help in directing these investigations, and likely much remains for it to do. From the point of view of these functions, anatomy has at this time little in the way of explanation to offer.

In these days, when we are set about by tracings made in a variety of ways, by instruments that detect numerous different physiological activities, and by the effort to understand the meanings of the tracings once obtained, one must insist and insist strongly that all this is but machinery, nothing but a means to an end. It is as aids in understanding the heart in health and disease that this cumbrous apparatus is called into being. The tracings which they yield will be exceedingly barren, unless the effort to interpret them from the standpoint of anatomy and of physiology, both normal and abnormal, is constantly made.

[42] Untersuchungen über das Atrioventrikular bundel im menschlichen Herzen, Fischer, Jena. 1910.

[43] Loc cit.

REVIEWS

JOINT TUBERCULOSIS. By LEONARD W. ELY, M.D., Consulting Orthopedist to the County Hospital, Attending Orthopedist to the Children's Hospital, Denver, Colorado; formerly Surgeon to the Sea Breeze Hospital, and Consulting Orthopedist to the Roosevelt Hospital, New York City. Pp. 243; 72 illustrations and a colored frontispiece. New York: William Wood & Co., 1911.

THIS is a very interesting book. It was begun by the author as a clinical study, but finding this inadequate to explain the phenomena of joint tuberculosis, he turned to the pathology, and, from an examination of 72 specimens from 64 patients, has come to some conclusions which must be regarded as of far-reaching importance if their truth be substantiated by further observation.

He found both osseous and synovial lesions as the primary focus, the latter very rare in children, but much more common in adults. Obliterating endarteritis was observed as a frequent characteristic in these tuberculous lesions.

The localization of tuberculous foci in the epiphyses of children he explains solely by the presence there of red marrow. Where red marrow exists there is a predisposition to the development of tuberculous lesions; and where there is no red marrow the bone is almost immune to infection by tubercle bacilli. Other explanations, he says, such as the lack of terminal anastomoses predisposing to embolism, do not explain. If red marrow can be converted into yellow marrow, tuberculous lesions will heal. He regards lymphocytic aggregations around tubercle bacilli not as the *result*, but as the *cause* of the tuberculous focus; lymphocytes, he contends, as well as connective tissues which contain epithelial, epithelioid, or lymphoid cells, are the natural food of tubercle bacilli; where these elements are not already present, tubercle bacilli do not thrive. He doubts the existence of primary fascial tuberculosis because there exist in fascia no cellular elements suitable for the nourishment of tubercle bacilli.

From these pathological inferences—for at present they can scarcely be said to be more—the author finds a ready explanation of and indication for treatment. *Rest* is the main therapeutic indication, and it succeeds not because of either traction or fixation, which

are mere secondary means of procuring local rest, but simply because it abolishes the function of the joint; and as the function of a joint depends on the existence of red marrow and synovia, the disappearance of these structures, which is encouraged by disuse, promotes cure of the disease; since, where they are not, joint tuberculosis cannot exist. Cure which follows operation is obtained by securing ankylosis (*i. e.*, joint rest); it matters not how little tissue is removed, nor how much tuberculous material is left behind; so long as bony or firm fibrous union is obtained a cure will result, because ankylosis will cause disappearance of red marrow and synovia, without which joint tuberculosis cannot exist. He dilates on the futility of seeking to obtain cure by removal of all the tuberculous tissue; this is absolutely impossible. Resections should be done with the sole idea of securing ankylosis. Cure following excision of the hip, in which ankylosis does not occur, he attributes to the resulting pathological dislocation, which abolishes the joint tissues as such quite as surely as does ankylosis. Curettement and gouging he regards as useless always, and generally as harmful.

From these general principles of surgical treatment, the author proceeds to specific indications. Operations in children are condemned, because they are crippling, and the disease, if taken in time, usually is easily cured without. He seems to be partial to the weight-bearing treatment of hip tuberculosis by means of the short spica of Lorenz, because it promotes ankylosis; and if the disease in any joint is once cured by ankylosis, malposition, if present, can be corrected by osteotomy. As the disease, even when apparently cured by firm ankylosis, is in most cases not really cured, but merely indefinitely quiescent, he condemns, and we believe with entire justice, attempts to secure motion by arthroplasty in tuberculous hips. In adults ankylosis should be secured by operation before secondary infection renders amputation necessary; for without ankylosis or amputation cure need not be expected.

If sinuses are present, with secondary infection, tubercle bacilli can live in the walls of such sinuses; but if an uninfected sinus leads to an uninfected tuberculous joint, its walls will be free of tuberculosis. Hence, before operating on joints with secondarily infected sinuses with the idea of radical cure, it is desirable first to secure closure of the sinuses.

There is an appendix to the book, consisting of case histories which seem to be entirely useless for either pathological or clinical study, owing to the incompleteness with which they are recorded. References to literature throughout the volume should have dates of publication added, as only thus can the reader know whether the authority quoted is still worthy of credence. Clinically, the book is sketchy and incomplete. Pathologically, it is highly suggestive, but not entirely convincing. We shall hope for a second edition supplying these defects. A. P. C. A.

FOODS AND THEIR ADULTERATION. By HARVEY W. WILEY, M.D., Ph.D., Chief Chemist U. S. Department of Agriculture. Second edition; pp. 641; 98 illustrations. Philadelphia: P. Blakiston's Son & Co., 1911.

IN undertaking to review a book such as Dr. Wiley has written, the reviewer must at the outset confess either to a working knowledge of the subject or to absolute ignorance of the whole field. He pleads guilty to the "soft impeachment" of the latter.

To the reviewer, whose task at the present writing is one laid in pleasant ways, the work is the first of its kind which has come to his notice, and his memory fails to recall an instance where an author has so interestingly developed a table of contents which at first blush seemed so dull. To pretend that, at one reading alone, one is in a position to criticise justly a book of such magnitude were presumptuousness indeed, so that here is recorded nothing more than general impressions.

In the main this second edition follows closely the general lines of its predecessor, except that the rules and regulations for the enforcement of the Food and Drugs Act have been omitted.

The author, we fear, presumes too much on the knowledge of the medical man at least, when he offers "such wide distribution" of these rules as a reason for the omission. For the expert, perhaps, but for the medical world at large, who should certainly possess this book, we feel that the reason is not wholly sound. The place left vacant by the deleting of this very important part of the first edition has been divided between a new section on infants' and invalids' foods and one devoted to simple tests for ordinary adulterations.

These two sections have claimed the reviewer's close attention. The former is valuable, but it is questionable whether its insertion in a book of this nature is a particularly happy choice, inasmuch as the work is dedicated to a consideration of foods and their adulterations. We think the section with which Dr. Wiley has seen fit to replace that spoken of above would find a more appropriate environment in works devoted more especially to dietetics. It adds little to the volume unless the possessor of the latter be of the laity, who wishes in one book to have as complete information regarding foods as possible.

The part on detection of food adulterations is written especially for the great mass of people called the general public, but we fear that Dr. Wiley, in his zeal for the cause of the greatest good to the greatest number, has endowed the general public with unusual intelligence when he says of the "simple tests," that "anyone without the training of the professional chemist" may practise them. We very much fear that not every housewife would make much out of the test, for instance, given on page 611.

This book, which must be regarded as an expression of Dr. Wiley's

monumental governmental activities, is a classic. His great work under the Department of Agriculture is so well known that all classes of people regard the name of "Wiley" as one to conjure by. So great has been his work and so vast his field of endeavor, that few realize concretely just what he has done. With becoming modesty, the writer has submerged himself in his book, but they must be blind, indeed, who cannot see that such a work could not have been written without the brilliant researches of Harvey W. Wiley.

It is a valuable volume for all those interested in the science of foods, and, while not indispensable to the practising physician, should not be overlooked by him if he wishes to keep abreast of a question which is claiming more and more attention from the world at large, more familiarly known as the General Public. E. H. G.

THE NERVOUS LIFE. By C. E. PARTRIDGE, Ph.D., Formerly Lecturer in Clark University. Pp. 216. New York: Sturgis & Walton Company, 1911.

THIS is a first-rate work. Within the last few years there have been many popular books on the different "mental worries" and other nervous phenomena, which, according to their authors, seem to be the burden of the human race. The author approaches his work from the standpoint of both disease and health, and argues that the same principles of living are applicable to both. He first takes up the question of the normal life of the individual and the causes which tend to bring on a nervous condition, and then discusses the cure by normal readjustment through normal living. Dr. Partridge has treated the matter in a thoroughly commonsense fashion, and, after all, there is no higher praise than this.

The reviewer, a neurologist, modestly disagrees with the following: "The day has come when we can no longer go to the doctor to be cured of all our ills. Ills have multiplied faster than the doctor's medicines, and personalities have grown so varied and complex that everyone must, to a certain extent, work out his own salvation. It is, indeed, in the most intimate and personal parts of one's life, where neither physician nor other outsider can be competent to advise, that the most pressing of problems are to be found and the best work of self-study can be done." It is true that ills have multiplied faster than doctors' medicines, but then it must be recalled that the up-to-date physician who understands the modern psychological method of treatment of nervous diseases does not give a medicine for every ill. He knows better. He treats the patient. Again, it is all well enough to state that the most pressing

personal problems must be settled by one's self; but suppose the person is not competent to settle this question by himself, what then? Would it not, after all, be best for the patient with mental ills to go to a competent physician who can show him how to solve these problems?

Even such books as this cannot settle all questions for all persons. As a matter of fact, no better argument can be given for the increase of nervousness than the quantities of books which have been published and the many cults which have arisen. Every day one is confronted with some new "pathy" or new method of curing disease. This is partially because many physicians do not understand or do not realize that to treat nervous diseases one should treat the person, and by treating the person one does not mean giving medicines, but handling the patient psychologically; but the principal reason for the growth of osteopaths, Christian scientists, and others is because human nature, at least so far as the neurologist sees it, is frail. (The reviewer, who is a disciple of Bernard Shaw and incidentally of his "Doctor's Dilemma," does not claim this as an original discovery.) If the doctor were to promise that he could cure every and all diseases as definitely as does the Christian scientist and the osteopath, and if he had the ever-present and most splendidly conceived loop-hole that the Christian scientists have—that is, if one does not get better one does not have sufficient faith—then perhaps we would be on a par with them, but Heaven forbid! T. H. W.

Die Behandlung der Frauenkrankheiten. The Treatment of Diseases of Women. By J. Veit, M.D., Professor and Director of the University Clinic for Women at Halle. Pp. 242; 34 illustrations. Berlin: S. Karger, 1911.

This book begins with an observation so sensible that one wonders that it should be mentioned, and yet so essentially practical and useful that it lies at the foundation of all success in treating the diseases of women. Veit urges that in these cases the patient be treated from the objective standpoint only, and that the subjective element in the case be reduced to the lowest possible terms. When one considers how misleading are the symptoms often reported honestly or otherwise by women, and into what serious error they sometimes lead, this caution will be appreciated.

The book begins by treating of disinfection, the use of instruments and minor methods of treatment before proceeding to the operative side. Veit urges that before examinations strict antisepsis should be observed, a caution which is often neglected. He still seems to have considerable faith in the so-called "local treat-

ment" of women's disorders, illustrates the various sorts of sounds and applicators, and includes among his local treatment intra-uterine injections for endometritis, and electric vibration or electric massage.

In abdominal section he uses Trendelenburg's posture and varies the incision in accordance with the nature of the case. He differs radically from many American surgeons in his custom of leaving the abdominal cavity as dry as possible after operation. He makes no mention of introducing salt solution for absorption in the abdominal cavity. To prevent infection he surrounds the edges of the wound by large metal specula, which keep the abdomen open widely, and from the illustrations they should prove exceedingly useful. He would use drainage only in those cases where bacteria found in the abdomen are virulent, and where there is abundant material for their growth and nourishment. He endeavors to close the abdomen as soon as possible, believing that the admission of air for a long time may result in fresh bacterial invasion. The after-treatment which he advises is of the simplest variety. He allows the patient to get up early after operation, even in cases where the heart and bloodvessels are diseased. He uses salt solution freely by the bowel, and, if the patient goes on normally, removes the stitches in ten or twelve days. Vaginal puncture and incision, incision of the cervix and anterior vaginal hysterotomy are described and illustrated. He urges that a fair balance be struck between conservatism and the ambition to operate. The interests of the patient only must decide the choice of treatment.

In treating disorders of the external genital organs, he recognizes leukoplakia as a white thickening of the mucous membrane of the vulva, which is rightly termed kraurosis vulvæ when it surrounds the entire aperture. Laceration of the perineum is included in diseases of the external organs, and in complete lacerations he illustrates and practises the transverse flap method of Schröder. Under the head of diseases of the vagina he treats chorio-epithelioma, although this is almost invariably of uterine origin.

In endometritis, the subacute variety, he urges that care be exercised that no new infection be added, and that the physician wait until the infection has subsided, without sign of pelvic or abdominal involvement, before doing anything to the endometrium. Absolute rest and simple dietetic treatment are required in the first stages. In gonorrheal endometritis he would practise dilatation of the cervix after the initial stage had subsided, and the application of chloride of zinc to the interior of the uterus. Should the case prove obstinate, he would practically destroy the endometrium to prevent the recurrence of the infection. He would never practise curetting for catarrhal endometritis only, because of the presence of the discharge. He recognizes the protean character of endome-

tritis and its symptoms, and especially the pain which patients who suffer from this condition so frequently describe.

In the treatment of prolapse he describes plastic operations of the vagina, and illustrates them. There is nothing new in his methods. Amputation of the cervix rather than a conservative operation is recommended.

In treating myomata of the uterus, in some cases he prefers anterior hysterotomy and vaginal enucleation; in others the vaginal extirpation of the uterus is practised. Doyen's method of the abdominal extirpation of large tumors is illustrated and advised. It seems to him safer to remove the entire uterus where the tumor is of considerable size; where the tumor is small he operates through the vagina. In doubtful cases he prefers the upper operation, and tries, if possible, to leave at least one ovary in young women.

In treating cancer of the uterus, he employs formol solution on cotton to disinfect the vagina before operation. He has also had good results with vioform powder on gauze. He dissects away the the bladder from the uterus by the finger, and thinks it of great importance that this should be completely and carefully done. In most cases he operates through the vagina, closing the edges of the incision in the peritoneum as carefully as possible, and endeavoring to bring the peritoneum together over the upper end of the vaginal wound. He considers wounds and injuries to the bladder as among the most frequent accidents of the operation. He would also dissect out lymph glands as thoroughly as possible.

In discussing parametritis and perimetritis, he lays stress, as do most Germans, on treatment by baths and electricity, and especially electric baths in those cases of chronic parametritis which are not good subjects for operation. Ovariotomy is briefly but clearly described. He has occasionally removed ovarian tumors through the vagina. He would remove the Fallopian tubes in all cases of malignant disease where their condition is dangerous to the patient's life, and where there is reason to believe that serious disease would develop in the future. Where pus is found in both tubes, a radical abdominal operation is advised. In tuberculous cases he operates as little as possible, believing that general and dietetic treatments are preferable. A discussion of the diseases of the urinary passages closes the book.

In brief compass, 242 pages, Veit gives a clear and well-digested account of conservative gynecology at the present day. The book is valuable for its excellent balance, its clear and concise statements without padding, and may be taken as the mature expression of opinion of an intelligent observer. It is without bibliography, making no reference to other literature. Its illustrations are not abundant, but clear, and it is presented in the cheap paper binding, so commonly used upon the continent. E. P. D.

Old Age Deferred. The Causes of Old Age and its Postponement by Hygienic and Therapeutic Measures. By Arnold Lorand, M.D. Second edition; translated, with additions by the Author, from the Third German Edition; pp. 472. Philadelphia: F. A. Davis Company, 1911.

In a critique of Lorand's book one must bear in mind that the work has been written not only for the physician, but also for the layman (to whom, by the way, the publishers have freely advertised it). It is, therefore, not a scientific treatise on old age, but a charmingly personal series of "Plaudereien," in which sound common sense is found side by side with not a little exaggeration. The purpose of the book is to show the causes of psychical and physical decay, especially that coming on prematurely, and to indicate the ways in which the conditions characteristic of old age may be prevented or cured. Old age, in the author's opinion, is the result of disturbance in the function of the ductless glands, primarily the thyroid, but also the sexual glands, the pituitary body, the suprarenals, the pancreas, and the liver and kidney, which latter the author also includes among the ductless glands. There is hardly a disease which Lorand does not in some way connect with the thyroid. Old age he considers incomplete myxedema; indeed, one might say that the whole book is built around this particular thesis. He traces a strong connection between the thyroid and the sexual glands, and over and over again dwells on the apparent relation between markedly developed and long preserved sexual power and longevity. Like Sajous, whom he quotes freely, he holds that the opsonins are nothing more than thyroid secretion. Fever in infectious diseases is due to increased activity of the thyroid. Diminished activity of the thyroid predisposes to tuberculosis; a statement hardly consonant with the fact that in many cases of tuberculosis symptoms of hyperthyroidism are present. It follows quite naturally from the importance Lorand gives to the thyroid in pathological processes that he should look upon thyroid extract as almost a panacea. It is this advocacy of thyroid extract, and the stress laid upon the thyroid and other glands throughout the book, that the reviewer finds extravagant. For the sections dealing with diet, clothing, hygiene of the skin, and exercise, he has only praise. These chapters may be read with profit by physician and layman. While a teetotaler himself, not from principle but from distaste, Lorand is opposed to such narrowmindedness as prohibiting even the smallest amount of alcohol to those who only take it in the greatest moderation, solely on the ground that there are some good-for-nothings who can never take it without getting drunk. With regard to tobacco, he believes that two or three light cigars a day, never before meals, can do no harm save in exceptional cases. Though a bachelor, he nevertheless believes in the marriage state as a factor conducive to long life.

The author's knowledge of medical literature is vast; particularly gratifying are his abundant references to American writers. The references to German articles are often given in such a way that it is difficult to tell whether the paper referred to is German or Welsh. Stylistically, the book possesses a great deal of charm, and is characterized by a strong personal note, unusual in medical works.

D. R.

Introduction to Therapeutic Inoculation. By Carmalt Jones, M.A., M.D., M.R.C.P., Assistant Physician and Director of the Department of Bacterio-Therapeutics, Westminster Hospital, London, England. Pp. 165; 11 illustrations, and 5 plates. London: Macmillan & Co., 1911.

The contents of this little manual are divided into three parts, the first comprising 88 pages, dealing with the principles of inoculation therapy, with a short historical note; the second, of 41 pages, being a summary of methods and results obtained in the administration of vaccines; the last section, of 26 pages, being devoted to a detailed description of the technique employed in the preparation of the apparatus and in the making of vaccines and opsonic determinations.

This is the most satisfactory small treatise upon this subject that has yet appeared. It is distinguished by lucidity of expression and moderation of statement. Especially in the presentation of the results of treatment there is preserved a scientific poise which has been lacking in most publications by vaccine enthusiasts. The estimation of the opsonic index is commended both as an aid in diagnosis and as a control for therapeutic work but is conceded to be unnecessary for the clinician in many instances. A list, too long for enumeration, is given of diseases of the skin, the alimentary and intestinal tracts, of joints and bone, of lymphatic glands, of the genito-urinary tract, and of the eye and ear, and, in many, very considerable series of cases are adduced to show the expectation of cure or betterment under vaccine treatment. Much of the work is personal, but amplified by a few of the more reliable reports from the literature. One puts down the book feeling that in the birthplace of this method of treatment there has arrived a fair approximation of the value of this form of therapeusis, and that while hopes of miraculous cures are not justified in the majority of bacterial diseases, there yet exist good grounds for the employment of specific bacteriotherapy in infective conditions, particularly those of chronic and resistant nature.

D. B. P.

TEXT-BOOK OF MASSAGE. By L. L. DESPARD, Member and Examiner Incorporated Society of Trained Masseuses. Pp. 279; 203 illustrations, some colored. London: Oxford University Press, 1911.

MISS DESPARD has written with a lucidity and simplicity that suggests long and patient teaching. The abundant illustrations are well chosen. Much of the volume is given over to anatomy and physiology, but the remainder is mostly devoted to massage and considers the subject thoroughly as far as it goes. There is one matter of increasing importance which is neglected, and this is the treatment of tender areas that are so common in many parts of the body; they are usually called indurations, though familiarly known as "sore spots," and any statement which conveys the impression that such areas require gentle treatment is erroneous; their recognition and removal by the Swedish users of manual therapy is the one feature that makes theirs the system *par excellence;* for half a century the Swedes have written of these treatments, and for some years back the matter has been carefully considered in English literature, so that lack of knowledge upon this subject is hardly excusable.

Furthermore, it is to be regretted that some irregular practitioners have "discovered" these treatments and are employing the methods to their profit and to our chagrin; no other subject within the realm of manual therapy stands so urgently in need of widespread recognition. The book offers unusual aid in surgical conditions, and this is commendable. Since bandaging and electricity are considered, it appears that a section on mechanical vibratory massage would be germane to this work; however, this is unimportant, and the omission cited is the only just criticism to be offered against this excellent volume. N. S. Y.

HAY FEVER AND PAROXYSMAL SNEEZING. VASOMOTOR RHINITIS. By EUGENE S. YOUNG, M.D. (Edin.), Physician to the Manchester Hospital for Consumption and Diseases of the Throat. Pp. 147; 2 colored plates. New York: Wm. Wood & Co., 1910.

THIS is a well-written, instructive, and rather unusually accurate treatise on certain of the nasal neuroses. The book contains 147 pages, 85 of which are given up to the subject of hay fever, 35 to paroxysmal sneezing, and 7 to idiopathic rhinorrhea. The arrangement of the book is good, each of the subjects is dealt with in a systematic way, and there is a rather full general index. We are glad to see that the author has not omitted to put in references to

the literature that he has apparently read while reviewing the subject. It would have been better if the references had been indexed at the ends of the different chapters instead of at the bottom of each page, as they would then have been easier to consult. A rather disproportionally large part of the work is given up to the etiology of hay fever, and while he criticises fairly and in detail the different views and theories and gives with clearness the pros and cons of each, even after a careful reading, one is left with a great deal of uncertainty concerning the causation of the disease. As a matter of fact, this is at present about the extent of our knowledge concerning the etiology of hay fever. The treatment outlined is fairly extensive and seems to cover the whole field rather thoroughly. There is, however, an almost complete lack of detail concerning the various surgical procedures recommended, with the exception of the cutting of the nasal nerve and the removal of the tubercle of the septum, two operations which the author himself has devised, both of which seem to be still in the experimental stage. The illustrations are unimportant. On the whole, the book is a careful, well-written, up-to-date review of the subject with which it deals. G. B. W.

A Report on Hemoglobinuric Fever in the Canal Zone: A Study of its Etiology and Treatment. By W. E. Deeks, M.A., M.D., Chief of Medical Clinic, Ancon Hospital, C. Z., and W. M. James, M.D., Physician, Ancon Hospital. Pp. 177; 6 charts. Department of Sanitation: I. C. C. Press, Quartermaster's Department, Mount Hope, C. Z., 1911.

Of the publications following the increase of interest in black water fever which has succeeded upon the establishment of our modern knowledge of malaria, there are none within the knowledge of the writer which are of more importance to the subject than this monograph of Drs. Deeks and James. It is based upon the statistics of Ancon Hospital, running over the five years from September, 1905, to September, 1910, during which time more than 40,000 cases of malarial fever were dealt with in this institution, along with 230 cases of hemoglobinuric fever during the same period.

In their careful, logical, and complete analysis of the statistics before them, the authors point out that in the epidemiology of malaria and hemoglobinuric fever the periods of maximum intensity coincide; that hemoglobinuria as a whole prevails in direct proportion to the occurrence of malaria as a whole; that it prevails among a race in proportion to the susceptibility of that race to malaria and to the actual amount of such malarial infection in a given race; and that its prevalence bears no such relations with the prevalence of any other of the important infections met in the Canal Zone.

The authors are of opinion that in the Canal Zone (and inferentially elsewhere) hemoglobinuric fever has as its predisposing cause a prior malarial infection, that usually this is a prolonged or repeated infection, but that occasionally a single acute attack may induce this predisposition. They believe from the statistics which they employ that estivo-autumnal infection is particularly conducive to such a predisposition, and suggest that in part at least this fact may underlie the geographical discrepancies between the occurrence of malaria in general and hemoglobinuric fever. They acknowledge the probability of some unknown second factor operative as a determinant agent, and their records bear out the common contention that occasionally quinine may act as this second factor. They do not believe with Manson, Craig, and others that ordinarily this second factor is some unknown intercurrent infection, but suggest, in a theory which they propose, that it is some hemolysin developed and accumulated within the body of the subject in the previous period of the infection by the malarial hematozoa. This is the one weak part of the study, as is acknowledged by the writers, who, however, in academic argument, offer very rational grounds for not accepting Manson's surmises. Aside from this, no one may successfully cavil over the presentation made by Drs. Deeks and James. In the Canal Zone surely, and by inference anywhere else, hemoglobinuric fever is a manifestation of malaria; and it cannot be a misnomer to apply to it the old term of "malarial hemoglobinuria." But that the determining factor which acts in conjunction with the malarial predisposition is itself a product of the malarial infection, direct or indirect, is not proved. It is a permissible tentative assumption, to be verified or discarded when our knowledge is more advanced, just as the Mansonian idea of a complicating infection; and the writer feels that the study offered by Drs. Deek and James on the whole favors their inference.

Space does not permit one to present the discussion of this contention; but it is as easy to pick flaws and ask pertinent questions in regard to the theory of the authors as it is to deny the existence of a complicating hemolytic infection because it has not been demonstrated. There are analogies which are appealed to in support of the latter idea; in the history of Texas fever in cattle immune Southern cattle with Piroplasma bigeminum in their blood become hemoglobinuric when experimentally infected with rinderpest; and there is a growing feeling that the Anaplasma marginale found in the secondary access, when hemoglobinuria occurs, in cattle is not, as Smith and Kilbourne originally supposed, a phase of Piroplasma bigeminum, but in reality a second protozoan infection. Further study is essential, and this should not be limited to mere microscopic observation of the blood, but to bacterial culture from the blood, spleen, and allied organs as well. There are a number of arguments, for example, by which a second analogy could be erected

in the case of yellow fever, based on a view the writer has personally favored for a long time, by which the unknown protozoön of the disease is directly responsible only for the primary febrile access; and bacterial infection by bacillus x., Sanarelli's bacillus, or others of the so-called hemorrhagic group, enters secondarily to determine the secondary phenomena, including the jaundice, hemorrhage, and renal faults in which a fatal end is more common than in the primary phase. Hospital study would be more easy with a view of excluding such ideas than the experimental efforts necessary to prove the presence and malarial identity of a special hemolysin in cases of blackwater fever; and, it would appear to the writer, should be seriously considered by the Isthmian medical corps in continuance of the study which this work of Drs. Deeks and James so excellently summarizes and presents. Unquestionably these gentlemen and the general corps of Ancon Hospital, whose results they employ in their analytical study, have placed medical science under obligations to them; and the writer, in his partial hesitancy to follow them, by no means wishes to detract from the value of their work, but to suggest a line for future study with the view of verifying or correcting their present attitude. A. J. S.

Diseases of the Joints and Spine. By Howard Marsh, M.A., M.C. (Cantab.), F.R.C.S., Master of Downing College and Professor of Surgery in the University of Cambridge, Consulting Surgeon to St. Bartholomew's Hospital, and to the Hospital for Sick Children, Great Ormond Street. New and enlarged edition, thoroughly revised by the author and by C. Gordon Watson, F.R.C.S., Surgeon to the Metropolitan Hospital, Assistant Surgeon to St. Bartholomew's Hospital, etc. Pp. 632; 106 illustrations and 12 plates. Chicago: Chicago Medical Book Company, 1910.

This popular monograph appears in its third edition considerably enlarged, and presents in most sections the latest knowledge available on the subjects discussed. Over five hundred pages are devoted to diseases of the joints as such, and nearly one hundred to those of the spine.

Beginning with accounts of synovitis and injuries of the joints, the authors discuss in turn the general aspects of the acute arthritis of infants; of tuberculous, syphilitic, and gonorrheal arthritis; arthritis as seen in various infective diseases and septic arthritis; arthritis deformans, acute rheumatic arthritis, and arthritis in gout; "Charcot joints," joint changes in syringomyelia and hemophilia; newgrowths, cysts, and loose bodies in the joints; and ankylosis, with its treatment. The individual joints are next taken up in order; and Part I closes with chapters on congenital disloca-

tion of the hips, coxa vara, hysterical joints, interosseous pressure in joint disease, bone setting, movement, and massage.

In Part II, diseases of the spine, are discussed tuberculosis, malignant disease, spondylitis deformans, and necrotic spine.

Among the most interesting chapters are those dealing with infectious forms of arthritis. Though perhaps a clearer clinical distinction between infectious and dystrophic joint diseases could be drawn than has been done by the authors, their accounts of "subpyemic infections" are of great value; by this term they understand certain obscure pseudorheumatic joint lesions, seldom recognized, which resist all treatment until some source of toxin supply (dental caries, sinus disease, vaginal or uterine infection, etc.) is eliminated.

Of the dystrophic joint lesions, which they still confuse under the general term of arthritis deformans, they recognize two main classes —rheumatoid arthritis, in which synovial lesions predominate, and osteo-arthritis, in which bony lesions are conspicuous. Marsh and Watson seem not to have recognized as a distinct clinical and pathological entity the disease known in this country as the atrophic arthritis of Goldthwait and the metabolic osteo-arthritis of Nathan; yet certain features of their "rheumatoid arthritis" undoubtedly belong to this class, while others, which are confused with these, as surely belong among phenomena not of dystrophic but of infectious arthritis.

Apart from these questions of classification, which we believe could and should have been more satisfactorily solved, the volume affords the best guide to the pathology, diagnosis, and treatment of joint diseases at present to be secured in the English language in such compact form. A. P. C. A.

Taschenbuch der Pathologischen Anatomie. By Prof. Dr. Med. Edgar Gierke. I. Allgemeiner Teil; pp. 143; 69 illustrations. II. Spezieller Teil; pp. 207; 58 illustrations. Leipzig: Werner Klinkhardt., 1911.

This book is best described as an enlarged compend of pathology, covering the subject as usually taught in the medical school. It is intended to be used as an aid in taking accurate notes at lectures, and for this purpose wide margins have been left on each page. The text is usually concise, clear, and accurate, and the typographical work and illustrations are excellent. Although it is the intention of the author that the book shall supplement rather than supplant the lecture and text book of pathology, we feel that owing to its completeness it will tend to fulfil the latter purpose for many students, and hence the value of the book from a pedagogical standpoint is questionable. B. S. V.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Serum Treatment of Influenzal Meningitis.—Wallstein (*Jour. Exper. Med.*, 1911, xiv, 73). Since more accurate studies on spinal fluid have been made, an increased number of cases of influenzal meningitis have been found, almost all of which have been fatal. Almost all cases are due to an influenzal bacteremia. The organism grows in the subdural space and is swept through the blood. The organism was cultivated on agar slants for twenty-four hours, then washed off with salt solution, and two such cultures, 2 c.c. in all, were injected into the canal of a monkey, giving a disease, fatal in thirty-six hours to four days, and comparable to that in man. A goat was now treated with living organisms for eighteen months, when opsonins and agglutinins appeared in his serum, but the serum is not bactericidal in vitro. This serum was effectual in securing recovery if injected into the spinal canal twenty-four hours after inoculation. The bacilli are more freely engulfed by the leukocytes, their growth and eruption into the blood hindered. To be successful in the human disease frequently repeated applications of the serum to the spinal canal will be necessary. The diagnosis can usually be made by immediate microscopic study of the fluid.

The Effect of Atropine on the Pulse during the Administration of Digitalis.—Selberberg (*Proc. Roy. Soc. Med.*, Lond., 1911, iv, 192) discusses the effect of atropine upon pulse rate in cases under treatment by digitalis. It is not yet definitely known how digitalis slows the heart, but it acts best on mitral cases of rheumatic origin that have developed auricular fibrillation and arrhythmia, while the senile type

of cardiac degeneration, those with a regular rhythm, and the tachycardia of fever do not respond so well. Lewis considers it due to a partial block, and that cases with a prolonged A-C interval, that is, with a delay in conductivity, will become slower on digitalis. But clinically, the cases with rapid irregular action, that is, with a short conduction time, become slower. Cushing thinks that digitalis increases inhibitory action of the vagus and prevents many impulses reaching the ventricle. Is the action mainly vagal, or are the conducting fibers of the auriculoventricular bundle themselves, or is the heart muscle lowered in irritability due to improved nutrition? In the senile type there is loss of inhibitory power of the vagus, and so atropine has little effect; also the cardiac musculature is so degenerated that nutrition cannot improve it much. By action of atropine the effects of vagus inhibition could be removed and so one of the possible factors would be cut out. The patient's pulse was studied at rest, under atropine alone, under digitalis, and under the drugs combined. It was found in the rheumatic cases with rapid heart that the rate was slowed by digitalis, and on administration of atropine, while the rate was increased, it in no case reached the original rate before drugs; if the effect had been due solely to vagal inhibition, it is fair to suppose that following atropine the old rate would have been reached. There are thus two component actions of digitalis, one vagal and the other on cardiac tissue, and they vary in different conditions. In the cases of auricular fibrillation that give high increases of pulse rate on the administration of atropine, digitalis works its best, for following digitalis atropine has almost no effect in raising the rate; that is, most of the effects of the digitalis are on the cardiac musculature. These cases, as a rule, do well and may even resume work again. By the study of pulse rates following atropine with and without digitalis, it is possible to find out whether digitalis is acting upon vagus or cardiac tissue.

Pathology of the Dyscrasic Edemas.—Débove (*Presse Méd.*, 1911, xix, 517). While edema due to mechanical cause has long been differentiated from that due to a chemical change in the blood, it is well to remember that the blood composition is kept constant by the kidneys. An excess of salt or water is quickly eliminated in health by the organs acting as a selective filter and removing the superabundant ingredient. But the excretion of a concentrated toxic fluid by the kidney may endanger the organ. So in the diseased body it is usual to find the superabundant toxins distributed not alone in the blood, but in the general body fluids. For example, if one ligates the ureters and then injects a rabbit with some dyestuff, this material will not be recoverable from the blood, but from the general body. As the toxins can only remain in the body fluid in solution, they are diluted and result in edema, which thus appears to be a defensive reaction against toxins, and preserves the chemical constitution of the blood intact. In typhoid fever and pneumonia, for example, the patient loses little in weight in spite of high fever, because of edema that is not recognizable because it is so general. In the diuresis of convalescence the toxins are rapidly poured out by the kidneys and weight is lost. This rapid outpouring of toxins could, in pneumonia, be spoken of as a chloruria, because chlorides had been retained to make the toxic solution physiologically

normal and are now excreted rapidly. Not only does edema save the kidney from excreting too highly toxic fluids, but as antibodies are present in all transudates, the toxins are catabolized in the tissues and so rendered innocuous. Probably the pathogenesis of edema is the same in nephritis. Nephritis is largely due to a hematogenic infection. Frequently the fact is overlooked that the causative agent persists even if the kidney lesion makes no progress. Here the organism protects itself from the assault by edema in hydropic nephritis and by polyuria in the anhydropic. Clinically, in the hydropic form, it has been observed that a disappearance of edema has been followed by an exacerbation of the symptoms caused originally by the toxins, a fact that can be explained only by supposing the elimination of a too highly concentrated urine. But while Widal and Javal believe the edema of nephritis to be due to a primary retention of chlorides through kidney impermeability, Débove thinks it a primary retention of toxins. The blood and lymph contain the same amounts of chlorides before, during, and after nephritis, and it is highly probable that water and salts are retained to make the toxins dilute enough, also isotonic. When salt is excluded from the diet the edema is reabsorbed and gradually excreted. Sodium chloride is one of the simplest things for the kidney to excrete in health. In disease this power is somewhat impaired, but by no means so much as is the power of urea excretion. He thinks of flooding the kidney with a highly toxic urine. In this toxicity there is no reason to believe that sodium chloride plays any important part. In the interstitial form the organism tries to secure elimination by polyuria because the toxins are different and have acted upon different kidney structures. While many types of edema are mechanical in origin, we cannot afford to overlook the primary chemical change in the blood as is found in cirrhosis of the liver.

Functional Diagnosis of the Liver.—F. Falk and P. Saxl (*Zeit. f. klin. Med.*, 1911, lxxiii, 131) point to the fact that while amino-acids have frequently been found in the urine in large quantity in hepatic disease, practically no attention has been paid to the occurrence of the more complex nitrogenous bodies (polypeptids). The authors, therefore, undertook a study of the amount of amino-acid nitrogen and of peptid nitrogen in cases of primary liver disease and also in cases where the liver was affected secondarily. To determine the peptid N, they used the formalin titration method of Sörensen. As Falk and Saxl have previously shown, this method, as modified slightly by them, gives results which, though not absolute, are sufficiently accurate for clinical purposes. The studies of Falk and Saxl show that hepatic disease in general causes an increase in the relative quantity of both the amino-acid and the peptid N. Ordinarily the two are increased proportionally, but exceptions to this are quite frequent. After feeding glycocoll, they find no changes in the nitrogenous fractions in patients with normal livers; with hepatic disease, and particularly cirrhosis, they observed a great increase in the peptid N fraction.

The Blood Findings in Epidemic Cerebrospinal Meningitis.—Rusca (*Deut. Archiv f. klin. Med.*, 1911, ciii, 235) has made a rather complete study of the blood in nine cases of epidemic cerebrospinal meningitis,

of which six were fatal. At the beginning of the disease there is a leukocytosis, due mainly to an increase in the number of the polynuclear neutrophilic cells; the lymphocytes may be slightly increased or decreased. During the course of the disease, there occurs with each aggravation of the symptoms both a relative and an absolute increase of the polynuclear neutrophiles. During the decline of the acute symptoms there is a corresponding drop in the relative and absolute number of these cells. Thus, if one plots the lymphocyte and polynuclear neutrophile curves, it is found that they diverge with a recrudescence and tend to become approximated during recovery. In the cured cases, Rusca found a crossing of the polynuclear neutrophilic and lymphocytic curves, the lymphocytes becoming more numerous. Following a simple lumbar puncture, the author observed a fall in the leukocyte count. This fact should be remembered in those cases treated with serum, lest a similar occurrence should be attributed to the serum. In 2 of the cases which recovered, the eosinophiles were greatly increased, both absolutely and relatively. Mastzellen were lacking in all the fatal cases shortly before death. In 4 of his cases the author saw the meningococcus in the stained blood film, and in one of these a blood culture made immediately after studying the film yielded a positive culture.

Colloidal Nitrogen in the Urine in Cancer.—S. Mancini (*Deut. Archiv f. klin. Med.*, 1911, ciii, 288) has examined the urine for colloidal nitrogen according to the method of Salkowski. The twenty-four-hour specimen was always used. When alkaline in reaction, the urine was acidified slightly with acetic acid. Albumin, when present, was removed before examining for the colloidal nitrogen. The percentage of colloidal nitrogen in normal urine, taking the total nitrogen as 100 per cent., is about 3.56, according to Salkowski. Mancini found an increase of the colloidal nitrogen in cancer, the average being 6.48 per cent. of total N. He finds, however, that this increase is not specific for the urine in cancer, since a similar result may be encountered in pneumonia and pleurisy as well. Indeed, there may be an increase in all those diseases in which there is a continuous absorption of exudates or transudates, such as pneumonia, pleurisy, anasarca from whatever cause, cirrhosis of the liver, and purulent processes. An abnormally large proportion of colloidal nitrogen is, therefore, not diagnostic of cancer, but it may be of great aid in arriving at the correct diagnosis.

Irregularity of Feeding and its Effect on the Stomach.—Külbs (*Ztschr. f. klin. Med.*, 1911, lxxiii, 47) studied experimentally the effects of irregularity in feeding and also the time intervals between feedings which may be endured without loss in weight. The experiments were all carried out upon cats, and Külbs believes his findings may have some bearing on human pathology. The results he obtained are as follows: (1) If one gives a cat as much meat daily as it cares for, the animal soon regulates the quantity consumed, avoiding an excess. (2) Animals fed every second, third, or fourth day eat rather less that two-, three-, or fourfold the quantity of a daily ration. They do not lose weight, however, so long as they are fed regularly. (3) Slight irregularities in the time of feeding cause no disturbances. (4)

If the feeding hours are very irregular, death frequently follows with rapid loss in body weight. There is found a greatly dilated stomach or, less often, a subacute gastro-enteritis. (5) Occasionally, when the animals are fed regularly at long intervals, they die with atony of the stomach and rapid emaciation. (6) These observations may, perhaps, be correlated with the fact observed in man that the human stomach is frequently upset when the meals are taken at very irregular intervals.

The Diagnostic Value of Diastase in the Urine. — E. Marino (*Deut. Archiv f. klin. Med.*, 1911, ciii, 326) reports a quantitative study of urinary diastase in various diseases. He used the method of Wohlgemuth. The author finds (1) that the excretion of diastase in the urine is greatly lessened in nephritis and in diabetes mellitus. (3) In pancreatic disease the urinary diastase is increased in quantity. This, the author believes, is a very important sign of pancreatic disease. (3) As a functional test of the kidney, the quantitative estimation of diastase is valuable. (4) In pernicious anemia and in secondary anemia the diastase of the urine is markedly decreased. The diminution seems to be greater in pernicious than in secondary anemia, though the number of cases studied was too small to formulate a rule.

The Rate of Regeneration of Blood Platelets.—W. W. Duke (*Jour. Exper. Med.*, 1911, xiv, 265) has been able to render the blood of dogs practically free of platelets by withdrawing 200 to 300 c.c. of blood from the carotid artery, defibrinating it completely, and then reinjecting it intravenously. A repetition of this procedure six to ten times reduces the number of platelets to a minimum. He finds that animals thus deprived of the greater part of their fibrinogen and platelets display a marked tendency to bleed. After the practical removal of platelets from the blood, their regeneration is very rapid, amounting to about one-fifth of the normal number daily. From observations on human beings, Duke believes that the life cycle of the platelets is a matter of only a few days.

The Production, Life, and Death of Crescents in Malignant Tertian Malaria.—D. Thomson (*Annals Trop. Med. and Parasitol.*, 1911, v, 57) has studied the production, life, and death of crescents in treated and untreated cases of malignant tertian malaria by means of an enumerative method, the details of which are to be given in a forthcoming report. His results are summarized as follows: (1) Crescents are produced from the ordinary asexual spores of *P. falciparum*, due to a development of immunity toward the latter. (2) They develop somewhere in the internal organs and then appear suddenly in the peripheral blood. (3) The period required for their development is about ten days. (4) Crescents do not generally live more than a few days in the peripheral blood. (5) Crescents may be present in the peripheral blood during periods as long as eight weeks, not because the individual crescents survive for that time, but because their numbers are constantly replenished from surviving asexual forms. (6) Fresh broods of crescents come into the circulating blood daily, or every other day, or irregularly, according as the asexual sporulations occurring ten days before were quotidian, tertian, or irregular. (7) Quinine

has no direct destructive action on crescents, either during their development or afterward, but it destroys the asexual source of supply. (8) Quinine reduced the crescents to numbers less than 1 per c.mm. of blood within three weeks, provided it be given in daily doses of 20 to 30 grains. (9) Quinine in small doses tends to increase the crescent production (?) by favoring the development of immunity to the asexual parasites. (10) Methylene blue in doses of 12 grains daily reduces the number of crescents, and would seem to have some direct destructive action upon them.

Antityphoid Vaccination in the Army.—J. R. Kean (*Jour. Amer. Med. Assoc.*, 1911, lvii, 713) reports the wonderful sanitary record of the Maneuver Division of the Army at San Antonio, and compares the statistics with those of one of the camps in 1898. The most important features of his report deals with typhoid fever prophylaxis by means of typhoid vaccine. Eight thousand and ninety-seven men were vaccinated. In no case was the operation followed by serious results, and in 90 per cent. of the cases the reaction was mild or absent. In the entire division there was only one case of typhoid fever. "This patient, a private in the hospital corps, had not completed his immunization, having taken only two doses. The case was very mild, and would perhaps have been overlooked but for the rule that blood cultures were made in all cases of fever of over forty-eight hours' duration." During the time covered by this report 49 cases of typhoid fever, with 19 deaths, were reported in the city of San Antonio. Compared with the typhoid morbidity and mortality at Jacksonville, Fla., in 1898, the results at San Antonio show the extent of the advance. In Jacksonville, among 10,759 men, there were 1729 certain cases of typhoid fever (including the probable cases of typhoid, there were 2693), of which 248 resulted fatally.

The Leukocytes in Malaria: A Method of Diagnosticating Malaria Long after it is Apparently Cured.—D. Thomson (*Annals Trop. Med. and Parasitol.*, 1911, v, 83) has made many daily observations of the total and relative leukocyte counts in malaria, extending over long periods of time and after the patients were apparently cured. His findings are remarkable and unique. They are accompanied by numerous charts. The summary, in Thomson's own words, follows: (1) During active malaria the number of leukocytes in the peripheral blood is decreased. During quiescent malaria, and in cases apparently cured by treatment, the leukocytes in the peripheral blood are much increased. (2) During the rigor and temperature in malaria the mononuclear leukocyte percentage (more especially that of the large mononucleated variety) is low. With the fall in temperature, however, the mononuclear percentage rises very high, sometimes even to 90 per cent. of the total leukocytes. This fluctuation in the percentage of total mononuclear leukocytes occurs also long after continuous quinine treatment, and is observed for months and even years (?) after the last attack of fever. (3) In these apparently cured cases of malaria the mononuclear percentage is lowest at the time of the day at which the rigor and fever occurred during the previous active malaria; and, moreover, at this time there also occurs a very marked leukocytosis, which continues only for a few hours. The leukocytes reach numbers

as great as 30,000 to 50,000 per c.mm. of blood. On one occasion they were as numerous as 125,000 per c.mm. Two hours later they had fallen to 22,000 per c.mm., and in eight more hours they were only 6000 per c.mm. This case showed a regular daily periodic variation in the number of leukocytes, averaging from about 6000 per c.mm. to 50,000 per c.mm. The height of the rise always occurred about noon. This was the time at which the rigor and fever, which was quotidian, were wont to occur previously. This postmalarial leukocyte phenomenon occurred always without exception in the 40 cases examined, and would therefore seem to be an infallible sign of previous malaria, as, so far, it has not been observed in any other disease. (4) It would appear that large numbers of malarial parasites on sporulating cause a leukopenia, while a very small number on sporulating cause a leukocytosis.

Albumin and Albumose in the Sputum.—E. H. Goodman (*Archiv. Int. Med.*, 1911, viii, 163) has studied the albumin and albumose content of the sputum in a number of pulmonary diseases, and finds that the presence of albumin is of less diagnostic value than is attributed to it by certain observers. While albumin is usually present in the sputum in pulmonary tuberculosis and absent in simple bronchitis, exceptions are so frequent as to destroy the value of the test to a great extent. In fact, Goodman met with albumin frequently in non-tuberculous cases. He finds in most cases that the albumin is associated with a positive test for occult blood which probably explains the source of the albumin.

SURGERY

UNDER THE CHARGE OF

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Experimental and Clinical Investigations Concerning the Effect of Fibrolysins on Cicatricial Tissue.—Sidorenko (*Deutsch. Ztschr. f. Chir.*, 1911, cx, 89) says that in the last five or six years contributions have frequently been made concerning the favorable action of thiosinamin and its derivatives. Sidorenko made investigations to determine the value of thiosinamin-fibrolysin therapy. Clinically the fibrolysin was employed in a series of suitable cases. In the laboratory the effects of the fibrolysins were investigated upon cicatricial tissue, the blood, and the lymph taken from the thoracic duct. The experiments

were made on dogs, rabbits, and white mice. In the histological preparations no effect whatever of the fibrolysins could be found. The lymphogogue effect of the fibrolysin is at the present time doubtful. From the fluctuation in the number of leukocytes found, the fibrolysin is not shown to be a specific means of producing a leukocytosis. The therapeutic dose is harmless and produces no favorable appearances. From a critical examination of the material of other authors and of his own, the clinical and experimental evidence allows the assertion to be made that fibrolysins do not exert a therapeutic effect upon cicatricial tissue.

Thrombosis of the Cavernous Sinus not of Otitic Origin.—Otto (*Deut. Ztschr. f. Chir.*, 1911, cx, 177) says that thrombosis of the lateral sinus is frequently of otitic origin, and rarely arises from a surface infection with a thrombophlebitis progressing into the cranial cavity. He reports a case in which a carbuncle of the back of the neck gave rise to a septic thrombosis of the cavernous sinus which was demonstrated at autopsy. From his study of the subject he concludes that the cause of the thrombosis of the lateral sinus is infectious in most cases. Alveolar periostitis and erysipelas play a conspicuous role in the etiology. Carbuncle of the back of the neck is a rare cause. The symptoms, besides those of general sepsis and those due to the causal disease, are the results of disturbances in the circulation of the sinus, rarely unilateral, since the thrombosis soon extends to the other side. For the diagnosis, of chief importance are: The eye symptoms (exophthalmos, chemosis, paralysis of the eye muscles, especially ptosis, changes in the eye grounds from stasis), with pyemic temperature. Thrombosis of the cavernous sinus can be assumed as certain, when these eye symptoms are bilateral. An infectious thrombosis of the cavernous sinus is a disease which almost always runs a fatal course, although spontaneous healing does occur. A prospect of saving the patient's life is offered by early operation, which should aim at emptying the sinus itself. Because of the difficulty of gaining access to the sinus, one should be very cautious in its performance.

Pyloric Stenosis in Infancy.—Richter (*Surg., Gyn., and Obst.*, 1911, xii, 568) says that it is evident that the abundant literature on the subject that has developed in the last ten years is resulting in the recognition of this disease as a widely distributed condition. Two types are generally recognized—one characterized by a spasmodic action of the normal or slightly hypertrophied pyloric musculature, the other by an hypertrophy of the circular muscle of the pylorus, which enlarges to such an extent as to produce a tumor mass which effectually blocks the pyloric lumen, causing a mechanical obstruction. Richter uses the term "pyloric stenosis in infancy" in a general sense to include all cases; and limits the terms "spasm" and "hypertrophy" to the above-described conditions. The symptoms begin during the first weeks of life, usually in the second, third, or fourth. The first symptoms to attract attention are vomiting, constipation, and loss of weight. The vomiting is of a peculiar propulsive type. In one case the vomitus was thrown a distance of four feet. Vomiting commonly is accompanied by diarrhea. In pyloric obstruction it is accompanied by constipation.

With the vomiting and constipation are all the usual accompanying evidences of mechanical obstruction found in the adult—rapid loss of weight, profound depression, though not suggestive of the collapse of gangrene. With the diminished ingestion of fluids the baby presents the shrunken appearance of excessive dehydration. The urine is greatly diminished and finally almost totally suppressed. The upper abdomen is full, tense, and bulging, and is made more prominent by a marked retraction in the hypogastric region. The bulging mass is due to the distended stomach, made more evident by the collapsed and empty state of the bowels. In cases with hypertrophy, there can be palpated a small, solid, and very freely movable tumor, above and to the right of the umbilicus. Three types of operation have been widely practised—division of the pylorus, pyloroplasty, and gastro-enterostomy. Gastro-enterostomy has been the operation of choice of the great majority of operators, and was performed in the eleven cases operated on by Richter. There was one operative death, and of the 10 cases that recovered, one has since died. It was a typical hypertrophic stenosis. There is a universal gain in weight following the operation. None of the nine babies living shows any evidence of intestinal disturbance.

Concerning the Behavior of the Intestine under the Influence of the Digestive Activity of the Gastric Juice.—Fiori (*Zentralbl. f. Chir.*, 1911, xxxiii, 890) conducted a series of experiments on cats and dogs to show that the jejunal wall is not damaged in any way by contact with the gastric juice. He believes that the tissues of the intestinal wall contain an antiferment, which is capable of resisting the proteolytic action of the pepsin. The first series of experiments consisted in simply attaching the intestine to the stomach by a continuous seroserous suture, without opening the stomach. In the second series, a portion of the intestinal loop was laid in the thickness of the stomach wall between the mucosa and muscularis, without opening the stomach. In the third series the same operation was performed as in the second, with excision of the muscular layer around the attached portion of the intestine. In the fourth series the intestine was attached to the stomach as in the first series, but the stomach was then opened and the stomach wall was then excised at the site of the attachment of the intestine. This was to insure against the constriction of the intestinal wall by the muscular ring in the stomach wall. In the fifth series an excised portion of the small or large intestine, with good vascularity, was laid in a corresponding deficiency in the stomach wall. In none of the seven dogs operated on in the last series, which lived from two to thirty-six days after operation, was any change observed in the transplanted piece of intestine. This was a positive proof of the resistance of the intestine against the digestive activity of the gastric juice. While in the first series no disturbances arose from the simple attachment of the intestine to the stomach by the continuous seroserous suture, in the second and third series it was shown that the gastric muscle surrounding the attached intestinal loop can cause severe disturbances of nutrition, which may lead to necrosis of the tissues enclosed. In the fourth series it was shown that the intestinal wall, when not under the ischemizing influence of the gastric muscle ring, can resist the digestive

influence of the gastric juice. As the result of a long series of chemico-physiological experiments, Fiori believes that there exists in the intestinal mucosa, as in that of the stomach, an antiproteolytic substance.

The Care of the Stump after Resection of the Stomach.—Polya (*Zentral. f. Chir.*, 1911, xxxviii, 892) says that of the various methods of treating the gastric and duodenal stumps after resection of the stomach, that of Kocher more than any other restores the normal anatomical conditions. Yet after an extensive resection with the best possible mobilization of the duodenum, the gastroduodenostomy can not be performed without tension, and this leads easily to suture insufficiency. When the gastric stump is too small and the anastomosis opening is placed in the posterior wall of the stomach close to the occlusion sutures, the intervening strip of stomach wall may necrose, as has been observed several times. In the Billroth I operation the danger of suture insufficiency is still greater. In the Billroth II operation regurgitation threatens, especially when the gastric stump is too small to permit a gastro-enterostomy opening of suitable size and position. The operation which Polya employs for exhaustive stomach resections where the Kocher method cannot be performed easily and without tension consists briefly in implanting the gastric stump in its whole extent, end to side, into a longitudinal opening in the upper loop of the jejunum, which is brought through the opening in the mesocolon. The advantages are as follows: The gastro-enterostomy is easily performed, and the gastric stump can be united to the intestine without any tension. The suture holds very securely and brings together in all parts broad serous surfaces. The most favorable conditions are provided for the emptying of the stomach contents, the communicating opening is very wide, is at the aboral end of the gastric stump, and provides a physiological direction for the passage of the stomach contents. The stomach discharges its contents into the upper part of the jejunum, so that there is no afferent loop, as is the case in Mayo's no loop gastro-enterostomy. The suture for closing the end of the gastric stump is avoided. Polya has performed the operation on 6 patients with extensive resections of the stomach for cancer. Two patients left the hospital cured. One seventy-year-old patient was completely well in five weeks, except for a small fistula which kept her in the hospital. Then erysipelas developed on the nose and extended over the whole scalp, and finally infected the small abdominal fistula. The patient died forty-nine days after operation with an acute retroperitoneal phlegmon. Three very severe cases which died one to two days after operation showed that the gastro-enterostomies healed without fault.

The Employment of a 1 Per Cent. Camphorated Oil in Peritonitis and its Effect in Preventing Adhesion Formation. — Hirschel (*Zentralbl. f. Chir.*, 1911, xxxviii, 1022) says that he was the first to employ camphorated oil for the treatment of the inflamed peritoneum in man, which he did in 1907. Others followed, some, especially the gynecologists using it not for peritonitis but as a preventive of it. It was then injected into the abdominal cavity forty-eight hours before the operation to increase the resistance of the peritoneum. Hirschel employs it only in very bad cases of peritonitis, mostly after per-

foration of the appendix, but also after perforations of the stomach and intestines. The purpose of this paper was to repeat briefly the technique which he follows. Every operation for diffuse peritonitis should be done as quickly and with as little interference as possible. The pus is best removed from the peritoneal cavity with dry or moist gauze pads as thoroughly as possible, although the peritoneum cannot be completely cleansed. The pus must be taken up on both sides, when necessary in the upper part of the abdomen, and especially in the pouch of Douglas. With a gauze pad on a long holder the warm 1 per cent. camphorated oil is spread over the whole abdominal cavity in excessive quantity, on the parietal and visceral surfaces and between the coils of intestine, so that all the serous surfaces are glossed with it. It may be poured into Douglas' pouch. The quantity used may be 200 to 300 grams. The abdominal wound is then closed to the drainage tube. The focus of the peritonitis must, of course, always be removed or rendered harmless. The camphor stimulates the heart, and this effect lasts a long time. The paralyzed intestine soon shows peristalsis, and soon after the operation gas is passed by the rectum. The frequent vomiting observed before the operation, ceases immediately. In one case, in which long after the introduction of the oil a complication led to a fatal termination, at the autopsy there was found everywhere a very smooth peritoneum which was covered with a fine layer of oil. No kinking or strong adhesions could be found. In one case, in which the oil had been employed for a diffuse peritonitis, several months later operation was necessary for an abdominal hernia. Except for one small omental adhesion to the scar, no further adhesions were found.

Extraperitoneal Embedding of the Omentum in the Kidney as a Therapeutic Measure, Especially as a Diuretic. — Torikata (*Deut. Ztschr. f. Chir.*, 1911, cx, 420) says that Bakes, in 1904, was the first to wrap with omentum the denuded kidney extraperitoneally, in a case of nephritis. Phocas decapsulated the kidney for ascites from liver cirrhosis, because he had observed that this operation, when done for nephritis (Edebohls), had a strong diuretic effect. Omi, in 1907, among other experiments on dogs, placed the left kidney intraperitoneally, fixed the omentum by sutures in a wound of the kidney, and showed that an excellent venous anastomosis could be obtained in this way. Isobe recently studied intraperitoneal omental embedding in the kidney, and came to the conclusion that this operation gave the best results up to the present time with relation to anastomosis formation, venous as well as arterial. Torikata recently treated a case of ascites with anasarca, by embedding the omentum in the kidney in its extraperitoneal position. After a study of the subject, he concludes that for anasarca from nephritis, when operative treatment is to be considered, extraperitoneal embedding of the omentum in the kidney is a better operation than the denudation or the surrounding of the kidney with omentum. In combating ascites from portal obstruction, most surgeons prefer the operation of omentopexy to the anterior abdominal wall. Torikata recommends very strongly his operation, which includes an omentopexy, and in addition has a diuretic effect. Finally, he concludes that his operation deserves undoubtedly the preference when hepatic cirrhosis and nephritis are combined in the same patient.

The Ideal Operation for Arterial Aneurysm; A Contribution to the Circular Suture of Vessels in Man.—Omi (*Deut. Ztschr. f. Chir*, 1911, cx, 443) operated on a case of popliteal aneurysm as follows: Under chloroform narcosis and with the limb rendered bloodless by an Esmarch tourniquet, an incision was made about 20 cm. long over the tumor. The aneurysm was isolated with little difficulty. The popliteal artery entered and emerged on the medial side of the sac. This was then opened and a large quantity of clotted and fluid blood escaped. The sac was extirpated as a whole with a short piece of the afferent and of the efferent portion of the artery, so that 4 cm. of the artery was removed. The popliteal vein lay external to the artery without a communication between them. After the application of forceps the tourniquet was removed. The two arterial stumps could be brought together easily by flexing the knee, and they were united by a Carrel-stitch circular suture. The arterial wall was markedly thickened and sclerosed, so that suturing with a fine needle was difficult. Before drying, the site of operation was protected by dropping on it repeatedly Lock's solution. After removal of the forceps and digital compression for a few minutes, no signs of hemorrhage from the suture holes could be seen. The wound was closed except for a gauze drain. The popliteal artery pulsated distinctly and the pulsation in the dorsalis pedis and posterior tibial were unchanged and the tissues everywhere were warm. The limb was fixed in the flexed position. On the next day pulsation could be felt in the posterior tibial and on the second day in the dorsalis pedis. Ten days after the operation the wound was healed and then the limb was gradually extended. On the twenty-first day the patient went about with crutches. Thirty days after the operation, pulsation in the posterior tibial and dorsalis pedis could be detected. The patient now walks without difficulty.

The Storing of Blood in the Extremities, its Influence on the Bleeding in Operations, and its Effect upon the Organism.—Zoeppritz (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, xxiii, 367) says it was known to the ancients that blood could be stored up in the extremities by applying a tourniquet near the trunk, and this method was employed for arresting hemorrhage especially from the lungs. They also recognized that it was not without danger. The method was also employed for hemorrhage from the nose, and in the last twenty years the indications have been extended to combating edema of the lungs, apoplexy, and disturbances of the circulation calling for blood letting. The tourniquet should be applied as close as possible to the trunk and with moderate tension, so as to occlude the veins with as little interference as possible with the arteries. In a muscular thigh it is often difficult to regulate the pressure, but it is more simple in the arm. The pulsation in the dorsalis pedis artery in the lower extremity, and in the radial in the upper extremity, can be felt at first, but in about ten minutes it cannot because of the complete stoppage of the venous current. After some time the early redness turns to a dark blue color, so that one is tempted to remove the tourniquet. But this should not be done. It is necessary to guard against too great loss of heat in the limb by wrapping it up well. From an extensive study of the subject, Zoeppritz concludes that by applying a tourniquet to the roots of the extremities by a suit-

able technique, about one-fourth of the total blood of the body can be stored in the extremities. To this bleeding into the extremities the body answers with more or less diminution of the blood pressure, increased frequency of the pulse, and disturbance of the breathing. The method may be employed as a prophylactic against hemorrhage during operations. It is to be recommended in operations on the brain, when there is no increase of the intracranial pressure, in operations on the spinal cord, and in other operations when severe parenchymatous bleeding is expected. There is no danger of a secondary hemorrhage. Some of the contraindications are brain pressure, arteriosclerosis, blood diseases, varicose veins, etc. The maximum of stored blood in the extremities, with a proper technique, is obtained on an average after one and one-half hours. A diminution of the force of the heart beat is to be recognized by the pulse after a long-continued application of the tourniquet, and an increase of the same on releasing the tourniquet. With the brain exposed, on releasing the tourniquet, the whole brain mass rises, and the pulsation is well established.

Concerning the Late Effects of Chloroform Narcosis.—Stierlin (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, xxiii, 408) says that while the dangers of chloroform narcosis are usually over with on the first signs of returning consciousness, this rule is not without exception. Fortunately the cases are rare in which, from one to several days later, threatening and usually fatal conditions arise, for which the chloroform is responsible. The results of investigations do not justify us in ignoring the existence of a permanent idiosyncrasy against chloroform poisoning, for in individual cases it may be of very great importance. It has been shown that such an idiosyncrasy may be transitory or may be due to a diminished resistance, as from certain diseased conditions. Such conditions are septic or suppurative processes, cases of autointoxication, principally in connection with torsions, strangulations, and incarcerations of abdominal organs (twisting of pedicles of ovarian cysts, volvulus, obstructed herniæ, omental or mesenteric cysts). The danger of chloroform in these affections increases with the intensity and duration of the narcosis, and most likely with the size of the twisted organ or strangulated portion of intestine, and is less with a brief, uncomplicated incarcerated hernia. The danger, however, is always so great that chloroform narcosis is very strictly contraindicated in all the above conditions and in pyosalpinx. In such cases the quantity of chloroform which would be borne by some men and many other patients without difficulty, would be sufficient to cause severe damage to the liver and kidneys, and subsequently the death of the patient. The causes of the decreased resistance to chloroform are to be found probably, partly in autolytic changes or abnormal internal secretions, which can aid the narcotic poison; partly in a previously existing degree of liver insufficiency, which from the effect of the narcotic may cause a deleterious accumulation.

The Motor Function of the Pyloric Sphincter and Pyloric Antrum in Dogs after a Transverse Division of the Stomach.—Kirschner and Mangold (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, xxiii, 446) found, after complete transverse division of the stomach in dogs,

thus separating the pyloric half from the influences of the vagus nerve and from its functional relationship with the cardiac half, that the tone of the pyloric sphincter and the rythm of the change between its closure and opening during the emptying of the stomach is completely normal. The increase in pressure due to contraction of the pyloric antrum, the rhythm, and the character of the antrum contraction remain unchanged. The functional coördination of the sphincter and antrum of the pylorus is preserved. The chemoreflex of the pyloric portion of the stomach, beginning in the duodenal mucus membrane, continues. Since the physiology of the dog's stomach is very much the same as that of the human stomach, we are justified in transferring the knowledge obtained in dogs to the human, where the clinical observations up to the present time do not contradict the results obtained in dogs. It is a striking fact that, as already mentioned, apparently normal stomach function is reëstablished very soon after the operation of tranverse resection of the stomach. This transverse resection with immediate union of the wound surfaces has not only the advantage of restoring the normal anatomical relations as much as possible, but it brings about a complete restoration of the physiological relations, since the regulative and motor functions of the distal portion of the stomach are not disturbed. To what degree pathological conditions of the sphincter and antrum of the pylorus, such as motor sluggishness or increased tone (pyloric spasm), existing before the operation, will be influenced by transverse division of the stomach cannot be determined by the results of the writers' experiments.

The Control of Bleeding in Operations for Brain Tumors.—Cushing (*Annals of Surgery*, 1911, liv, 1) says that one of the chief objects of concern in intracranial surgery should be the avoidance of any unnecessary loss of blood, for at best, in many cases of brain tumor associated with venous stasis, bleeding is likely to be so excessive as to necessitate postponement of the final steps of the procedure until a second or even a third session. The common methods of stilling blood by sponge, clamp, and ligature are largely inapplicable to intracranial surgery, particularly in the presence of bleeding from the nervous tissues themselves, and any device which serves as an aid to hemostasis in these difficult operations will bring a larger number of them to a safe termination at a single sitting, with less loss of blood and less damage to the brain itself. In addition to the more familiar tourniquet for the scalp, and wax for diploetic and emissary bleeding, suggestions are offered as to the use of gauze pledgets, dry sterile cotton, fragments of raw muscle and other tissues, as well as sections of organized blood clots for superficial meningeal bleeding, and silver "clips" for inaccessible individual points either in dura or brain. The successful consummation of any critical operation often depends upon seeming trifles. It is, however, the scrupulous observance of surgical minutiæ that makes possible the safe conduct of major intracranial performances.

THERAPEUTICS

UNDER THE CHARGE OF

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Influenzal Meningitis and its Serum Treatment.—Flexner (*Jour. Amer. Med. Assoc.*, 1911, lvii, 16) says that influenzal meningitis can no longer be considered a rare disease. Within a few months, in the United States alone, reports dealing with this subject have been published by Wollstein, Dunn, and Davis. All but 6 of the 58 cases thus far reported have terminated fatally. Wollstein has been able to induce in monkeys a severe form of cerebrospinal meningitis by the injection into the spinal canal of virulent cultures of influenza bacilli. An immune serum was then prepared from goats by repeated injections of virulent influenza bacilli extending over a long period of time. It has been found possible to rescue monkeys regularly from the fatal effects of the subdural inoculation of cultures of the influenza bacillus, through daily injection, by means of lumbar puncture, of the immune serum for three or four days. Flexner advises this treatment for influenzal meningitis in human beings in the same manner in which the serum for epidemic meningitis is employed.

The Present Status of Diabetes Mellitus.—Minkowski (*Med. Klin.*, 1911, vii, 1031) believes that the oatmeal cure is only suited to individual cases of diabetes and that the benefit derived from its use is often not permanent. However, he has seen remarkable results by this method and he does not hesitate to recommend it, especially for the severe type of the disease. He is of the opinion that the beneficial results obtained by the oatmeal treatment are due in part to the restriction of the protein intake. The restriction of the proteins in the diet reduces the metabolism as a whole and also eliminates them as a source of sugar production. He quotes Naunyn, who appreciated the importance of reducing the total metabolic processes in diabetes in order to secure a minimum excretion of glucose. For this reason, Minkowski thinks that it is wise to reduce the amount of muscular exercise in severe cases of diabetes. He also believes that the former strict withdrawal of carbohydrates in the treatment of diabetes is now being replaced by the opposite extreme, and deprecates this tendency.

The Treatment of Diabetes with Oatmeal.—Magnus-Levy (*Berlin. klin. Woch.*, 1911, xlviii, 1213) believes that the beneficial effects obtained by the oatmeal diet in diabetes are to be explained mostly by the absence of meat from the diet. He says that the oatmeal cure should always be preceded for a few days by a diet containing a minimum amount of bread—less than 50 grams. The oatmeal diet should continue for a period of three or four days and then be followed by one or two green vegetable days. This process is repeated if necessary, but

the treatment must not be continued for weeks at a time. Magnus-Levy says that this treatment is only necessary for the moderately severe and the severe cases. The method must be followed, but with great care as to details, and daily quantitative determinations of the amount of sugar in the urine are necessary to control the treatment. Magnus-Levy gives the details of the treatment in a case treated by this method. He says that equally good results may be obtained in some individual patients with rye or wheat meal instead of the oatmeal, but believes that oatmeal starch has certain unknown qualities that makes it superior to other starches for the majority of diabetic patients.

A Physiological Investigation of the Treatment in Hemoptysis.—Wiggers (*Arch. of Int. Med.*, 1911, viii, 17) says that the perusal of recent text-books on internal medicine indicate the chaotic state that the management of pulmonary hemorrhage is in today. Adrenalin, ergot, digitalis, and strophanthus have been recommended by some authorities because of their constricting action upon the pulmonary bloodvessels and the slowing of the heart beat. Others deny their efficacy because of the rise of blood pressure induced by them. Atropine has been advised on the assumption that the dilatation of the skin bloodvessels caused by it draws blood from the pulmonary circulation, while others have condemned it because of its accelerating action on the heart. Aconite, chloral, and chloroform have been frequently recommended, since they reduce the output of the heart and thus tend to relieve the pressure in the pulmonary circuit. The overdepression of both heart and the respirations are the chief reasons for their non-employment by other observers. Amyl nitrite and other nitrites have also been favored on the ground that they lower the pulmonary blood pressure by reducing pressure in the left auricle. They also cause acceleration of the heart that may more than counterbalance this fall in pressure, and for this reason are pronounced useless by others. Wiggers discusses in detail the theoretical basis of the experiments he performed, and gives his conclusions regarding the various remedies that have been more or less empirically recommended. He found that alcohol-free preparations of digitalis cause a rise of arterial pressure and an immediate increase of hemorrhage, owing to the increased output of the right ventricle and the constriction of the pulmonary vessels. They do induce a temporary fall in venous pressure and a reduction of venous hemorrhage lasting as long as the heart remains slowed. This is shortly followed by an increased pressure and hemorrhage when the slowing action is lost. The experiments showed similar effects with strophanthin as those observed with digitalis, except it failed to slow the heart, consequently no beneficial effect of strophanthin upon pulmonary hemorrhage, whether from arteries or venis, can be assumed. Ergotoxin temporarily decreases the pulmonary arterial pressure because of its depressant action on the heart. This is followed by an increased pressure due to a secondary augmentation of the heart. The pressure and hemorrhage from the pulmonary veins are permanently decreased, owing to a persistent constriction of the smaller vessels. The action of ergotoxin on the heart and circulation wanes as the loss of blood continues. Pituitary extract elevates the systemic

arterial pressure by virtue of its peripheral constriction and in spite of a weakening of the left heart. Pituitary extract also causes a fall of pressure throughout the pulmonary circuit because of a decrease in the amplitude of the contractions of the right ventricle. There was no effect upon the expirations except in severe hemorrhages when it sometimes lessened the amplitude of dyspneic respiratory movements. Large doses of chloroform cause a fall of pressure within the pulmonary circuit due to the depression of the heart aided by the diminished respirations. Small doses of chloroform lessen the respiratory movements in hemorrhage and so decrease the pulmonary pressure and hemorrhage without affecting the heart. The nitrites and nitroglycerin cause a general increase in pressure throughout the pulmonary circuit on account of the increased rate and amplitude of the heart, consequently they also cause an increase of the hemorrhage. They may cause a reduction of hemorrhage in the stage when they induce a reduction in the depth of the respiratory movements, which is a symptom of dangerous depression and is accompanied by a weakened systole of the heart. Wiggers concludes by discussing the application of these remedies to cases of pulmonary hemorrhage upon the basis of his experimental work. He says that the chief object of treatment is to promptly reduce the bleeding in the early stage by such drugs as lower the pressure within the pulmonary circuit. He says that this cannot be accomplished by vasomotor drugs such as nitroglycerin or nitrites, and that cardiac depressants, such as chloroform and pituitary extract, must be resorted to. If hemorrhage is continued until the heart is very rapid and the respirations accelerated, deep, and forcible, it is an indication that the heart and bloodvessels no longer react in a typical manner to certain drugs and that the anemia of the cerebral centres is being felt. During this stage it is important that the blood supply of the brain be not reduced by the drugs which check hemoptysis. Hence the drug that combines an ability to elevate systemic arterial pressure and simultaneously to lower that in the pulmonary circuit is the ideal physiological agent to employ during this stage. Wiggers says that, of the drugs investigated, pituitary extract is the only one that possesses his fortunate combination of actions.

Phenylcinchonic Acid in Gout.—Georgiewsky (*Deutsch. med. Woch.*, 1911, xxxvii, 1030) has employed phenylcinchonic acid in the treatment of gout because of its action in markedly increasing the excretion of uric acid in the urine. He says that the majority of patients so treated have shown an improvement in both the subjective and objective symptoms. These results have also been obtained by a number of other observers. The author gives the remedy in doses of 0.5 gram three or four times a day for periods of from five to ten days. No outward effects have been observed from its use.

Indications for the Vaccine Treatment of Disease.—Reiter (*Berl. klin. Woch.*, 1911, xlviii, 1235) says that vaccine therapy should never be resorted to in general infections. Local suppurations of all kinds, including local tuberculous infections, are most suitable for vaccine treatment. An autogenous vaccine gives the best results. Autogenous vaccines are absolutely indicated in infections due to the

colon bacillus. If the case is urgent, polyvalent vaccine should be used until an autogenous vaccine can be prepared. Reiter believes that it is most important to begin with small doses, and local reactions must be avoided. An interval of at least five days should elapse between injections. Furthermore, this interval should be lengthened if the dose of the vaccine injected is increased.

The Serum Treatment of Influenzal Meningitis. — Wallstein (*Jour. Exper. Med.*, 1911, xiv, 73) states that the injection of virulent cultures of Bacillus influenzæ into the subdural space of several species of lower monkeys is followed by the development of an acute inflammation of the meninges, corresponding in chemical, bacteriological, and pathological effects with influenzal cerebrospinal meningitis in human beings. Experimental influenzal meningitis in the monkey is a lethal disease, which terminates fatally in from thirty-six hours to four days after the inoculation. The injected influenza bacilli produce their effects through multiplication, in the course of which they penetrate from the subdural space into the general blood current, from which they may be recovered during life and at autopsy, as is also true of the spontaneous form of influenzal meningitis in man. By repeated injection over a period of many months of living virulent cultures of Bacillus influenzæ into the goat, an immune serum possessing moderate agglutinating and high opsonic power may be produced, which is capable, when injected into the subdural space, of arresting the progress of an experimental influenza meningitis, and of bringing about recovery in monkeys thus affected. As a result of the serum injection, the influenza bacilli in the meninges are more fully englobed by phagocytes, their number is reduced, their capacity of growth diminished, and the eruption into the blood arrested. Along with these effects go, hand in hand, cessation of the local inflammatory process and progressive amelioration of the symptoms of illness, to be followed usually by rapid restoration of health. In view of the highly fatal character of influenzal meningitis in human beings, the employment of an immune serum by subdural injection is recommended. Undoubtedly it will be necessary to apply the serum early and by repeated injections, by means of lumbar puncture, to secure beneficial results. The early application will, in turn be dependent on prompt bacteriological diagnosis, which can be made, as a rule, by the immediate microscopic examination of the cerebrospinal fluid without the employment of cultural methods. When possible, the microscopic diagnosis should be confirmed by cultural tests.

The Administration of Diphtheria Antitoxin by the Mouth. — Cumberlege (*British Med. Jour.*, 1911, cviii, 2637) sums up the points that, according to his experience, indicate that the administration of diphtheria antitoxin by mouth is superior to the usual method of giving it by injection. He says that results are obtained within a few hours and the action of the antitoxin is little slower if any than when it is given by injection. The dose required is also much smaller. Cumberlege has never given more than 4000 units at one time; his usual practice is to give an initial dose of 2000 units and to repeat this dose if necessary. He says that it is often a good plan to give the anti-

toxin in small repeated doses every two or four hours. Another advantage of this method is that there is less risk of sudden heart failure that sometimes results from the struggling of children to escape the needle. No patient treated by Cumberlege with this method has shown any evidence of serum sickness, whereas rashes or joint pains were frequently observed when the antitoxin was given by injection.

The Wheat Flour Treatment of Diabetes.—Blum (*Münch. med. Woch.*, 1911, lviii, 1433) says that when wheat flour is substituted for the oatmeal as given by the von Noorden method, there is no essential difference in the results obtained. The substitution of wheat flour for the oatmeal has many practical advantages, since wheat flour may be given in many different ways, but the methods of administering oatmeal are limited. Blum discusses the theory of the action of oatmeal and wheat meal in diminishing glycosuria. He thinks that the vegetable days serve to relieve the blood of the excess of sugar, and following this the individual's tolerance for starches increases. Another factor of importance is that animal proteid, especially meat, seems in some manner to diminish the power of the body to burn up the carbohydrates. For this reason meat is excluded from the diet when giving an oatmeal or wheat meal cure. Blum says that the milder forms of diabetes respond to this method of treatment more quickly than do the severe forms. It is often unnecessary to precede the meal cure with starvation vegetable days in the mild cases, and in severe cases it may even be dangerous to do so. The vegetable days should always follow the meal days in the severe cases. The mild cases can take large amounts of carbohydrates, usually from 200 to 250 grams, with an equal amount of butter, and in some cases from 50 to 75 grams of vegetable proteid or three or four eggs. He gives moderately severe cases 125 to 150 grams of meal, but allows them as much butter as he does the mild cases. The meal cure is of special value in the treatment of the severe cases with acidosis. In this class of patients care must be used not to give too large quantities of carbohydrates. Blum says that not more than 100 grams should be given at first. After a day or two this amount should be reduced to 50 or 75 grams for a few days, and then the diet should be restricted to green vegetables for a day or two. During the meal days, 125 grams of butter, 50 to 60 grams of vegetable proteid, and the yolks of from four to six eggs are also given. There is no definite rule as to the amount of carbohydrate to be given, but it should be diminished according to the severity of the individual case. Acidosis is much less apt to occur with the meal treatment of severe diabetes, and the glycosuria disappears more rapidly. Blum has treated thirty-five cases with wheat flour in place of oatmeal in the von Noorden diet, and says that the results have been equal if not superior to that obtained with oatmeal.

PEDIATRICS

UNDER THE CHARGE OF

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Further Reports on the Rumpel-Leeds Phenomena in Scarlet Fever.—In relation to recent articles on the Rumple and Leeds sign, it is interesting to note that ALBERT MAYR (*Münch. med. Woch.*, 1911, lviii, 1359) examined 100 cases taken from a skin clinic, in which there was no question of scarlet fever, to determine whether this sign was present in other cases. Twenty cases of this series gave an absolutely positive result. The technique was carefully followed out according to Rumpel and Leeds. Of the 20 positive cases, 14 were females and 6 males. They were of all ages, and there were no pathological skin conditions above or below the area of examination. Scarlet fever was absolutely excluded in every case. The typical hemorrhages around the elbow appeared in from three to ten minutes and lasted from two to four days. Mayr, therefore, holds that the formation of hemorrhages from compression of the upper arm can not be held pathognomonic of scarlet fever, since he has shown that it occurs also in cases with skin and venereal affections, and is especially strong in lupus, syphilis, eczema, psoriasis, and gonorrhea.

Hemorrhage of the Adrenals in the Newborn.—GEORG MAGNUS (*Berlin. klin. Woch.*, 1911, xlviii, 1119) reports a series of 124 infants who died either at or within eight days of birth. In 8 of these cases the necropsy revealed macroscopic hemorrhages in one or both suprarenals. Two of these 8 cases were delivered spontaneously, 3 by version, 2 were foot presentations, and 1 was delivered by Cesarean section. The labors in most of the cases were difficult. Three had asphyxia, and the Schultze method of swinging was employed. In all but 2 cases the infants died within eight hours of birth. The autopsy in these cases showed usually anemia and icterus, and in every case hemorrhage with free bleeding in one or both suprarenals. In some cases the suprarenals were surrounded by a large blood cyst from the hemorrhage. The author quotes a long list of writers who have reported this condition. All are agreed that the destruction of the parenchyma is most marked. The capsule is either unaffected or is secondarily so. The etiology of this condition is doubtful. Among a number of theories may be mentioned fatty degeneration of the adrenals, eclampsia in the mother, trauma during labor, and pressure of the liver on the vena cava. Materna believes in a hyperplasia of the parenchyma causing a disposition toward hemorrhage. It has been found by many observers that abnormal changes, such as congestion and hemorrhage, are almost constant in the adrenals of still-born infants and those dying shortly after birth. Clinically differentiated, one type exhibits progressive symptoms of peritonitis; one type is apoplectiform, with delirium, convulsion, and coma, ending within a few hours or days.

This is the most common form. The presence of icterus is noticed in a large number of the cases reported, but the production of this sign is problematical.

A Rheumatoid Condition of Measles in Infancy.——M. Feibelmann (*Münch. med. Woch.*, 1911, lviii, 1560) reports an acute, polyarticular inflammation occurring a few days after an eruption of measles in a six-months-old infant. The infant showed the typical symptoms and eruption of measles. There were no Koplik spots. The temperature was 39.3° C. Under treatment the eruption faded rapidly. Several days later the infant developed intense swelling and redness of the dorsum of the right foot and joints of the great toe, the dorsum of the left foot, the joints of the right hand, and the right elbow-joint. All the affected joints were intensely tender. Examination of the heart and mucous membranes was negative. The treatment consisted of aspirin internally and local application of aluminum acetate. The following day showed the same involvement of the right hip- and knee-joints. Sweating was not observed and the spleen was not palpable. The axillary and inguinal glands were not enlarged. By the third day the joint conditions began to improve and the temperature was normal. The leukocytoses was 12,000. In four or five days the symptoms had disappeared and the child had entirely recovered. At no time could any cardiac involvement be demonstrated. Feibelmann concludes that there was a direct etiological connection between this polyarticular affection and the measles which developed five days previously; in other words, he considers this an arthritis of measles. Acute articular rheumatism is a rarity in infancy, and some authors deny that it ever occurs in the early months of life. There was no evidence of tuberculosis, syphilis, serum disease, or gonorrhea as a causal factor in the case. The intense inflammatory reaction, the redness, and external tenderness in this case are not seen in a pneumococcus arthritis. Finally, the severe constitutional symptoms of a septic arthritis were entirely absent. Joint complications frequently occur in the various infectious diseases, such as scarlet fever. They are, however, extremely rare in measles, and Fritsch, in a recent search through literature for this particular complication in measles was able to find but 5 authentic cases. Feibelmann mentions 4 additional cases, 2 cases credited to Kompe, 1 to Spitzy, and 1 to Olinto, which, with his own case just described, make a total of 10 cases. In a number of these cases the condition developed finally into joint effusion or chronic arthritis.

Clinical Aspects of Acute Appendicitis in Children.—Harold Collinson (*The Practitioner*, 1911, lxxxvii, 61), in emphasizing the clinical difference between appendicitis in children and in adults, states that it is the commonest and most important surgical disease of the abdomen in childhood. Most of the cases occur between the ages of five and fifteen years. In children the appendix is comparatively larger, lymphoid tissue is more abundant, and there is a shortness and lack of development of the omentum. The causes of appendicitis are similar to those of adults, careless feeding and catarrhal diseases probably taking the lead. The difficulties in making a diagnosis in infant children are great. Pain, a constant symptom, is often ascribed to an

ordinary gastro-intestinal attack. Nausea and vomiting may be absent even in peritonitis. It is hard to determine and estimate abdominal rigidity. A rise of temperature is so common in children that this sign is not absolutely reliable. Fever in appendicitis usually begins some time after the initial pain. A sudden drop is a danger signal, and may mean gangrene or perforation. In gastro-enteritis, vomiting is earlier and precedes the pain. Abdominal pain is less severe and true abdominal rigidity is absent. It is a grave mistake to treat appendicitis with a purgative. The chest should be carefully examined in every sudden onset of illness in children because of the abdominal symptoms occasionally observed. There is no real rigidity in this case. The onset is just as sudden in intestinal obstruction as in appendicitis. Abdominal tenderness and rigidity are usually less marked, distention is earlier, and pyrexia is absent. The condition may occur during an attack of appendicitis from adhesions. A rising pulse rate disproportional to the temperature is a danger signal. Tenderness and rigidity are the most important symptoms we have, although they are often not marked. The prognosis in children is doubtful, and depends on the virulence of the affection and the method of treatment. Apart from early operation the prognosis in children under ten years is bad. Above five years, with early operation the outlook is good, below five years it is not always serious. The indiscriminate use of purgatives is a large factor in the fatal termination of many cases. In the treatment, a careful examination is imperative to establish a diagnosis. Having made a diagnosis of appendicitis, operation or the waiting method may be chosen. The Ochsner method of absolute starvation for four days is not applicable in children. The only safe course is operation, and this should be urged even during the first forty-eight hours because of the inability to predict the subsequent course of the disease, especially as in these patients the symptoms are so misleading and the margin of safety is small. During the second stage of the disease operation should be advised, but as little manipulation as possible should be observed. After the subsidence of a case the appendix should always be removed. The keynote of treatment is operative procedure at the earliest possible moment.

Early Cardiac Paralysis and Hemiplegia in Diphtheria.—Cresswell Burrows (*Brit. Jour. Child. Dis.*, 1911, viii, 311) reports a case of nasal and faucial diphtheria in a girl, aged four and one-half years, in which cardiac involvement appeared on the eighth day. Up to the thirteenth day the cardiac symptoms were distant first sound of the heart, vomiting, and disturbed rhythm of the beats, albuminuria. So far the treatment was adrenalin solution, 1 to 1000, ℥x every four hours. On the thirteenth day cantering rhythm, or *bruit de galop*, developed and vomiting continued. On the seventeenth day the heart was much dilated, pulse very rapid, but the cantering rhythm had disappeared. Tincture of digitalis in doses of 5 minims were now added to each rectal feeding every four hours. The pulse rate was 124. Three days later the pulse rate had dropped to 72, and in three more days the digitalis was discontinued. On the eighteenth day the pulse was still irregular, the heart still enlarged, but the heart sounds stronger. Albumin was still present in the urine. Up to the twenty-second day

the cardiac condition gradually improved, although vomiting still continued at intervals. There was some paresis of the left labial muscles, and nasal voice. Paresis of the sphincter vesicæ developed, and tincture of belladonna, ♏x, and adrenalin, ♏xx, were administered in the nasal feedings. On the twenty-sixth day reduplication of the second sound appeared, and lasted sixteen days. On August 4 external paralytic squint appeared. The knee-jerks were absent on the forty-second day. Three days later paralysis occurred in the left arm, and shortly afterward in the left leg. There was no aphasia. On the seventy-third day, thirty days after the onset of hemiplegia, the arm and leg were almost well. There remained only paralysis in the extensor muscle of the thumb and the peronei of the leg. The child was discharged in this condition. After four months of electricity and massage, the affected muscle had improved but still showed weakness. The knee-jerks were still absent. Very few cases of hemiplegia following diphtheria are recorded. Dr. Rolleston, in searching the whole literature, found only 65 cases. In the present case there were no mental symptoms, although some cases show motor aphasia. Cases of early cardiac paralysis in diphtheria are usually fatal. Among 326 cases of paralysis severe cardiac paralysis occurred in 33 instances. This form occurred in 10.1 per cent. of all forms of paralysis and in 2.4 per cent. of the total diphtheria cases.

The Specific Organism of Scarlet Fever.—A. E. Vipond (*Archives of Pediatrics*, 1911, xxviii, 564) publishes a preliminary report of his investigations in scarlet fever to determine a specific organism. He believes that the enlargement of the lymph nodes in infectious diseases is due to the irritation from the specific organisms of the diseases, the portal of entry being the tonsil. The infection is then carried to the lymphatic system. A number of organisms have been isolated in scarlet fever and claims set up for their specificity. Such are the coccus described by Class, of Chicago, and the streptococcus isolated by Gordon and Klein. Investigators, however, incline to the belief that the streptococci in scarlet fever are secondary invaders and not the specific organisms. Vipond, believing that the specific organism would be found in the lymph nodes, obtained lymph from enlarged glands in 7 cases of scarlet fever. This lymph, under strict antiseptic precautions, was inoculated into slants of Agar, blood serum, and broth. There resulted a raised white growth which turned out to be bacilli. This bacillus, when isolated, proved of rapid growth, and grew rapidly on all different media, including dextrose agar, blood agar, plain agar, blood serum, and broth. In each of the cases cultures of this same bacillus were obtained. Out of the 7 cases Vipond obtained a pure culture of this bacillus in 5 cases, 2 from inguinal nodes, 1 from axillary nodes, and 2 from anterior cervical nodes. Regarding this bacillus as the specific organism, he injected broth culture of it into monkeys, hoping to develop scarlet fever. The monkeys were all healthy and showed no glandular involvement before inoculation. The first monkey inoculated developed general involvement of the glandular system in forty-three hours. It became quite ill, and on the fifth day developed a red rash, a typical strawberry tongue, and died. The same bacillus was recovered from the enlarged glands. The other three monkeys

all showed the following symptoms after inoculation: Enlargement of the lymph nodes in the axillary and inguinal regions; engorgement and congestion of the throat; appearance of a red rash on arms, shoulders, and body; a tongue typical of scarlet fever, malaise, anorexia, and fever; free desquamation continuing as long as three weeks. The same bacillus was recovered from all three cases from lymph taken from an enlarged node. Inoculation of the recovered bacilli into a fifth monkey and two rabbits reproduced the same disease in these animals, with the recovery subsequently of the same bacillus. Koch's law was carried out to its fullest extent in these experiments. The monkeys and rabbits readily developed the disease. The shortest incubation period was two days, and the longest five days. The lymphatic nodes were unusually palpable within thirty-six hours. No suppuration in any instance occurred at the point of inoculation. Streptococci would likely have had this effect. Cultures show this organism to be a long bacillus with rounded ends, staining variably with Gram, and occasionally showing a beaded structure. Some cultures show sluggish oscillatory motility. The organism is an active spore former, the spores being endogenous. On sugar media it produces acid with gas formation. It coagulates milk with formation of acid. Vipond subsequently succeeded in producing scarlet fever in a monkey and in a rabbit by direct contagion from monkeys and rabbits suffering from that disease, and recovered the identical bacillus from their lymph nodes.

OBSTETRICS

UNDER THE CHARGE OF

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Vaccines in Puerperal Sepsis.—Polak (*Bull. Lying-in Hosp. N. Y.* December, 1910) has studied the influence of vaccines on puerperal septic infection. He finds that each case, whether following labor or abortion, must be studied individually, and that the determination to use vaccines will depend upon the evidence present if nature is competent or incompetent to circumscribe or localize the infection. Care must be taken to avoid interference with the genital tract during the acute stage to avoid the spread of the infection. Surgical interference should not be practised so long as the patient's general condition improves. All operations should be postponed until after the acute stage is passed. After the uterus is thoroughly emptied, at the time when infection develops, no further disturbance of the pelvic viscera should be practised. In the subacute stages vaccines may help by increasing the patient's resistance and powers of recovery. If drainage be employed, it should be extraperitoneal, if possible. Thrombophlebitis is considered a conservative process and should not be disturbed.

The Injection of the Serum of Pregnancy in the Toxemia of Gestation.—Rübsamen (*Zentralb. f. Gyn.*, No. 21, 1911) has endeavored to modify acute toxemia of pregnancy by injections of the serum of a pregnant patient. No results followed the treatment.

Tuberculosis in Pregnancy.—Schauta (*Monatss. f. Geb. u. Gyn.*, 1911, Band xxxiii, Heft 3, S. 265) discusses the question as to whether tuberculosis advances more rapidly during pregnancy and what should be done regarding the cases. The majority of clinicians believe that the disease progresses actively in pregnancy, 73 per cent. become worse, and 45 per cent. of tuberculous pregnant women die. Old cases relapse in 68 per cent. The change is most apparent some weeks or months after confinement, although such patients may, apparently, have been better during pregnancy. As regards the treatment of these cases, the German sanatoria find that only one-fourth of those treated after four years time have been able to earn anything at work; probably not 25 per cent. recover. Many sanatoria exclude pregnant cases, because of the unfavorable prognosis. The results of Norwegian observers show a mortality of 50 per cent. in cases treated in sanatoria. Among patients having every care, 29 per cent. grow worse during pregnancy. Children born of such mothers rarely live to be twenty. As regards the induction of labor in the first stage of tuberculosis, it is beneficial in 89 per cent.; in the second stage, in 83 per cent.; and in the third stage, in 25 per cent. Where pregnancy was interrupted in the first month, 91 per cent. improved. It is the duty of the physician then to interrupt pregnancy as early as possible. In addition it seems best to sterilize these patients, as tuberculous women conceive easily, and this had best be done by removing the Fallopian tubes.

The Treatment of Abortion Complicated by Fever.—Traugott (*Zeit. f. Geb. u. Gyn.*, 1911, Band lxviii, Heft 2) has observed 147 cases of puerperal patients having fever, of whom 58 had labor at term. Of these, 10 died, a mortality of 17.2 per cent. Of the remaining 89, 79 had abortion in the first half of pregnancy, usually from the first to the fifth month. Of these there died 13, 16.4 per cent. To investigate the mortality of these cases further, a study was made by bacteriological examination of the blood and uterine contents. Several groups of bacteria were found in the uterus, growing as saprophytes in the decomposing connective tissue and invading the living tissues. These germs produced simply a bacteriotoxic endometritis. The severity of the clinical symptoms depend upon the quantity of bacteria produced and whether or not the discharge has free exit from the uterus. Among these germs were colon and paracolon bacillus, yellow and white, staphylococci which do not produce liquefaction, Proteus vulgaris, sudodiphtheritic bacillus, and other bacilli. These bacteria are capable, either alone or in combination, of producing toxins whose absorption may cause severe symptoms. These bacteria, under favorable circumstances can be recognized in the blood, from which they often disappear without causing metastases. The most favorable time to recognize them is while the patient is having a chill, and they are also found in material removed from the uterus by curetting. When they have been diagnosticated by examination, the treatment consists in emptying

the uterus, and if no other bacilli are present, the patient immediately improves. The temperature falls to nearly normal, leukocytosis is less, chills cease, and the patient makes a speedy recovery. One can determine to empty the uterus or to let it alone in accordance with the germs found in its contents. The emptying of the uterus is done by the finger, and a list of 36 cases is appended, showing uninterrupted recovery. These cases were those in which there could be no doubt concerning the fact that saprophytic mucosis was the condition present in the uterus. When streptococci are present the conditions and history of the case are very different. Fever is present for a longer or shorter time after the emptying of the uterus, metastases develop in the genital organs or in other organs, and in a considerable number a fatal result follows. The recognition of streptococci puts the case in the category of those in which interference should not be practised, as each local disturbance lessens the patient's power of resistance and practically results in a fresh infection. Treatment is carried out practically as follows: If a primary examination shows no indication for emptying the uterus, a bacteriological examination of its contents is made by first disinfecting the external genitals, disinfecting the hands and using rubber gloves, introducing a sterile speculum and exposing the cervix, drawing it down with tenaculum forceps, carefully cleansing the surrounding tissues, and introducing Walthard's pencil into the uterine cavity. This pencil is seized with dressing forceps and the secretion of the uterus removed; twenty-four hours later growth of bacteria can be determined and an idea formed of the character of the bacteria present. Decision is then made to immediately empty the uterus or to wait. If the former course is chosen, the external genitals are thoroughly disinfected, and with the finger covered with a rubber glove, any debris, which easily separates, is removed from the uterus; the uterus is pressed down by the external hand, so that a complete and thorough examination of its interior can be made at the same time. The cavity is then packed with xeroform gauze and the vagina also tamponed with the same material. Intra-uterine injections are avoided, because of the danger of spreading the infection. Particles of retained material will be completely separated by uterine contractions and will come away with the gauze, and the uterus is kept well contracted by the administration of some preparation of ergot. To aid in this a firm vaginal tampon is also used. In cases where the cervix is closed after abortion, the effort is made to secure spontaneous dilatation by the use of the vaginal tampon. If this fails, a laminaria tent is placed in the cervix. Placental forceps and the curette are carefully avoided. In cases of streptococcus infection delay is practised, the patient is given absolute rest and the best possible diet, and if no bad symptoms develop, this form of treatment is pursued without interruption. Examination is made of the blood and uterine contents, and importance is given to the leukocytosis as expressing in some degree the patient's power of resistance. The effort is made to wait until the primary uterine infection has subsided, when the uterus is explored by the gloved finger, debris removed, and the gauze packing used as in the first instance. Instruments are never introduced within the uterine cavity. Should the patient suffer from hemorrhage, the effort is made to control it by tamponing the vagina firmly and giving some prepara-

tion of ergot. This treatment usually secures, within twenty-four hours, the expulsion of any retained portion, and if hemorrhage persists, the tampon is renewed and a strip of xeroform gauze introduced within the cervical canal. This tampon is renewed in accordance with the abundance of the discharge, and is used as often as is necessary. It is the rule to find any retained material spontaneously expelled under this treatment. In cases infected by both the streptococcus and diplostreptococcus and gonorrheal bacteria, the same treatment has proved, in his experience, successful. The question as to whether the same sort of bacteria are found in the vagina and uterus in these cases is one of no practical importance, as there is no difficulty in removing the contents of the uterus if reasonable care be taken by the methods already described. As regards the danger of this manipulation, in several thousand cases no accident has occurred. To contrast these results with those of curetting, in 11 cases of abortion or premature labor in which the lochial discharge contained streptococci, treated with the curette, 5, or 45.5 per cent., died.

The Correction of Unfavorable Presentations in Breech Labor Caused by Impaction of the Arm.—Sellheim (*Zeit. f. Geb. u. Gyn.*, 1911, Band lxviii, Heft 2) calls attention to the fact that many of these complications arise from artificial rotation of the child's body, which loosens the arm from its normal position across the chest. The effort should be made to avoid such rotation, so far as possible, and it should be accompanied by gentle massage of the uterus, following down the uterus from above. After expulsion has been secured, spontaneous as much as possible, no interference is necessary; the operator must introduce the hand as high as possible and dislodge the impacted arm under complete anesthesia.

The Source of the Amniotic Liquid.—Wohlgemuth and Massone (*Archiv f. Gyn.*, 1911, Band xciv, Heft 2) have studied the composition of the amniotic liquid, and find reason to believe that it cannot be regarded as a fetal product only. It cannot also be considered entirely as a transudate from the mother's body. It is, however, derived from the blood of the mother. The experiments of the writers show that a normal substance of high molecular concentration circulating in the mother's blood passes directly into the amniotic liquid, and any variations in concentration of the mother's blood directly have influence upon the specific gravity of the amniotic liquid. These and other considerations demonstrate that the mother's blood is in direct relation with the amniotic liquid. Exactly how close is this relationship we do not as yet know. It is, however, sufficiently ascertained that while the mother's blood does not directly participate in the amniotic liquid, it can transmit substances to this appendage of the fetus.

Glycogen in the Placenta.—Flesch (*Monatsschrift f. Geburts. u. Gynäk.*, 1911, Band xxxiv, Heft 1) has made investigations to determine the presence of glycogen in the placenta and in the glands of the uterine decidua. He examined 9 placentæ at full term, 1 at seven months, 8 from abortions from six weeks to five months, 1 from tubal pregnancy, and 5 specimens obtained by curetting. He finds that

the placenta at full term contains glycogen, but decidual tissues also contain it, although some cells may be found free from it. The fetal portion of the placenta contains less glycogen than the maternal. The greater number of villi of the chorion, at full term, are free from glycogen, and this substance is found most often in the connective tissue; the syncytium contains it frequently, but in very small quantity. The amnion and chorion are regularly found to contain a small portion. Especially noteworthy is the abundant quantity of glycogen in placentæ before full term. As the Langham's layer of cells disappears, glycogen in the fetal tissues also grows less in quantity. In the placenta at full term the maternal tissues contain by far the greater quantity of glycogen. This substance is also present in the uterine glands and in the uterine epithelia. In normal uterine epithelia glycogen was found in granules in the cells of the uterine glands. These granules surround the nucleus and disappear entirely toward the poles of the cell. In rare cases granules were found at the base of the cells, closely piled upon each other. In the normal mucous membrane the granules usually contain glycogen, and in no case was the mucous membrane of the uterus entirely free from glycogen. The uterine glands, however, differ greatly in the amount which they contain. Where the mucous membrane had been the site of inflammation glycogen was also found, and in greater quantity than in the normal glands. The uterine glands in the membrane of the pregnant uterus were rich in glycogen, although no difference could be detected between the compact and spongy layers. It is interesting to note that the amount of glycogen found in the various cells may be taken as an indication of the activity of the uterine glands, for the increased quantity of pregnancy suggests that this substance is of value in the nourishment of the pregnant woman. This substance is never to be taken as a degenerative product, but is the result of a physiological process. It was formerly supposed that glycogen existed in cells in a dissolved condition. Flesch, however, found this substance in granules of varying size and thickness.

The Technique of Extraperitoneal Cesarean Section.—Sellheim (*Monatssch. f. Geburts. u. Gynäk.*, 1911, Band xxxiv, Heft 1) describes efforts which he has made to simplify the performance of suprasymphyseal section. He has devised an instrument for grasping the fetal head, which he terms a "grasping lever," and which enables him to extract it from the uterus with the least possible disturbance of the uterine wound. He believes the best results are obtained by incising the uterus as low down as possible and in the median line. He believes that during the extraction of the child the abdominal tissues should be carried as far up as possible and held firmly in that position. The instrument consists of a solid handle separating into two blades, joined at the tips by a narrow portion. The blades diverge in a curved fashion and accommodate the average fetal head. The instrument is slipped over the head and the head slowly and cautiously raised out of the uterine cavity.

Serum Therapy in the Toxemia of Pregnancy.—Freund (*Zentralbl. f. Gyn.*, 1911, No. 27) has tried the effect of serum from pregnant animals injected intravenously in doses of 30 to 40 c.c. In 3 cases

of skin lesions occurring in pregnancy, prurigo, urticaria, and erythema, the result was very good, for, two hours after the injection the intense itching, irritation, and disturbance subsided and the patients recovered. The serum was also tried in some cases of eclampsia, in which, after the emptying of the uterus, the kidneys acted sluggishly and the chlorides were especially deficient in excretion. The best results were obtained, however, by prompt delivery, as in 497 cases of eclampsia it was found that those delivered during the first hour after the first convulsion showed no maternal mortality.

Bacteriological Examination of Patients Having Fever during Labor. —Sachs (*Zentralbl. f. Gyn.*, 1911, No. 27) believes that in patients having wounds fever is much more apt to occur, especially in the presence of hemolytic streptococci. As wounds and lacerations of the connective tissue develop, so the danger greatly increases. In these cases one must avoid operative interference, if possible, and choose that form of delivery which is attended by the least laceration and violence.

The Diagnosis and Treatment of Contracted Pelves. — Munro Kerr (*Surgery, Gynecology, and Obstetrics*, July, 1911) contributed a paper upon this subject at the recent meeting of the American Gynecological Society. He relies for comparative measurement of the pelvis and fetal head upon bimanual examination, pressing the head down into the pelvis with the right hand, while two fingers of the left introduced into the vagina note the degree of engagement. With the thumb of this hand the operator feels along the brim of the pelvis and estimates the degree of overlapping of the head. An anesthetic is occasionally necessary, and should the presentation be breech, the method still gives valuable information concerning the size of mother and child. Kerr believes that a careful measurement of the pelvis, both by hand and pelvimeter, should be made in all cases. An attempt should be made to estimate the size of the child's head, and especially the relative size of the head and the pelvis should be studied and made the basis of treatment. This examination should be made at the thirty-sixth week, and again at the beginning of labor, if the pelvic deformity is of moderate degree. In cases of medium deformity, with the true conjugate between 9.3 cm. and 7.5 cm. ($3\frac{3}{4}$ and 3 inches), the size of the conjugata vera is not the important factor in diagnosis, but the relative size of the head and the pelvis, which should alone determine the treatment. In these cases the treatment should be based upon the relative size of the fetal head and the maternal pelvis; if the choice of operation be based only upon the size of the pelvis, mortality and morbidity must result. One who is skilled in the method of examination described can almost always tell whether spontaneous labor may be expected. His experience in cases where the true conjugate was less than $3\frac{3}{4}$ inches, and where the forceps were applied, was so unsatisfactory that he now selects cases with great care, not applying the forceps until engagement and moulding have distinctly developed. In 130 cases with the true conjugate varying from 7.5 cm. to 8.7 cm., delivered by forceps at the earliest possible moment, the fetal mortality ranged from 15 to 46 per cent. In 22 cases of similar pelves, in which spontaneous delivery was procured in all possible conditions, the fetal mortality did not exceed 4.5 per cent.

Kerr would not entirely condemn the use of forceps at the pelvic brim, but believes that forceps should be used where the disproportion between the head and the pelvis is such that spontaneous delivery might have been reasonably expected, and the second stage of labor allowed to go on until there are very definite indications for hastening labor. When forceps are applied the head must be fixed, and the operator must expect to deliver with only moderate traction. No child should die or be seriously injured as the result of forceps delivery. In uncomplicated cases in which these accidents occur, the judgment of the operator has been at fault. Kerr, in recent years, has not performed Cesarean section late in labor, in cases that had been under his care through the entire time of parturition, and in which he had determined that spontaneous birth or forceps was possible. Craniotomy he has performed seventeen times in recent years, but in no case seen early in labor and under his care in the first stages of labor. Pubiotomy, he considers a reserve operation, which has a very limited field after spontaneous labor has failed to deliver, and one trial with forceps, with the patient in Walcher's position, if the pelvis be flat, has been made. His belief is that we have now reached the point in the practice of an obstetric surgeon where the number of pubiotomies will be in inverse ratio to a surgeon's diagnostic skill and judgment. Kerr's results in induced labor in hospital practice have not been satisfactory, for the early and late mortality with the children is slightly over 30 per cent. In domestic practice the results have been uniformly good. In selecting cases for this treatment he would choose those in which the true conjugate was not less than 8.1 cm., the pregnancy must have advanced at least to the thirty-sixth week, and the patient must be in her second or subsequent pregnancy, the first pregnancy ending in a test labor and showing liability to complications. In the thirty-sixth week the patient is examined under anesthesia and the relative size of the head and pelvis determined. If the head can be made to engage at the pelvic brim, labor should be induced. Craniotomy, Kerr thinks, cannot be limited strictly to cases where the child is already dead, but may be applied to cases in which the child has been injured or subjected to birth pressure to such a degree that its life has been seriously threatened. In cases suspected of infection, craniotomy has a mortality of about 8 per cent. In cases of dead or dying children it is the only treatment to be considered, when the pelvis is not highly deformed. In young healthy patients who are probably infected and the child already injured by birth pressure or efforts at delivery, craniotomy is probably the safest operation, where the pelvis is not highly contracted. If Cesarean section be chosen in infected cases, panhysterectomy is the preferable operation. Extraperitoneal section affords but one possible advantage over the classic section, that the cicatrix of a carefully stitched wound in the lower uterine segment may be firmer than one in the active contractile body of the uterus. In order to escape infection in suspected cases during Cesarean section, Kerr suggests that the placenta and membranes be pushed down into the vagina and not pulled up and delivered through the uterine wound. He is accustomed to very carefully wash out the vagina, cervix, and the child's head with liquid soap and normal salt solution. During Cesarean section the patient is placed on the operating table with her pelvis

slightly lower than her head. The skin is cleansed by iodine; the abdomen and uterus are opened in the usual manner; the abdomen carefully protected by gauze; the child is extracted by the feet. The operator now puts on a fresh pair of gloves, separates the placenta completely and covers it over with gauze, and then pushes gauze and placenta down through the cervix into the vagina. Several pieces of gauze are then pushed through the cervix above the placenta and removed from the vagina by an assistant.

Anteflexion of the Cervix and Spasm of the Uterine Ligaments in Relation to Retroversion, Dysmenorrhea, and Sterility.—Reynolds (*Surgery, Gynecology, and Obstetrics*, July, 1911) has treated cases of anteflexion of the cervix by preliminary dilatation and curetting and then measuring the length of the cervix and the external os to the point of flexion. The posterior lip of the cervix is divided by scissors in the median line up to this point. The angle between the line of the cut and the edge of the external os on each side is then sutured into the extreme end of the upper cut, after the manner of Dudley's method of discission of the cervix; two sutures, one on each side, are introduced. The anterior lip of the cervix is then seized by the volsellum and drawn strongly backward, putting the anterior wall sharply on the stretch. The vaginal wall is then divided transversely with the knife, just in front of the cervix, the cut being usually just wide enough to admit a finger and carried completely through the vaginal wall with the knife and scissors exposing the bladder. The finger is then passed into this cut and the bladder freed from the vagina and cervix well up toward the anterior surface of the uterus. A similar blunt dissection separates the anterior attachments of the vault of the vagina and the base of the bladder, well out to each side. It is important that this separation should be carried above the angle of the flexion. The edges of the vaginal wound are closed by transverse sutures, including nothing but the vaginal walls, thus lengthening the anterior vaginal wall. Profuse bleeding may be observed from the vaginal wall, but if blunt dissection be employed there is no other hemorrhage. In cases where careful examination has led to the belief that sterility is dependent on partial retention of secretions in the cavity of an anteflexed uterus, the operation has been very successful.

GYNECOLOGY

UNDER THE CHARGE OF

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Ovarian Causation of Uterine Myomata.—Seitz (*Münch. med. Woch.*, 1911, lviii, 1281) calls attention to the fact that the growth of the uterus is certainly influenced by the ovaries, since, when these are

removed the uterus atrophies. That this is not due to nervous influences is shown by the fact that if the ovaries are removed and a portion of one replanted in some part of the body, so that all nervous connections are severed, uterine atrophy does not occur. The author believes that the development of myomata is also dependent upon the internal secretion of the ovary, since no case is known of the development of myomata before puberty nor after the menopause. This relationship is also indicated by the reduction in size of myomata which takes place after castration, and after the destruction of ovarian activity by means of the *x*-rays. It seems probable, therefore, that the origin of myomata is due to the presence of some altered ovarian secretion.

Sea Bathing in Gynecological Affections.—Prof. Bossi (*Gaz. d. Ospedali e d. Cliniche*, 1911, xxxii, 707) makes a strong plea for what he terms "thalassotherapy" in the treatment of many conditions, sufferers from which are ordinarily subjected to serious and mutilating surgical operations, entirely too many of which he believes are being performed at the present day. He considers it the duty of teachers and heads of large clinics to advocate in many cases a return instead to the thermal and medicinal therapeusis of a generation ago, laying especial stress on the advantages of sea bathing in practically all chronic gynecological affections. In order to be effectual, however, this must be carried out under suitable conditions, which are: An equable mild climate with plenty of sunshine, warm water, and a smooth sea, conditions which, in Europe at least, are to be found only along the Mediterranean and Adriatic Seas and a very small portion of the Atlantic Ocean. The chief advantages obtained from sea bathing are due, according to Bossi, to breathing the sea air, to the actual immersion of the body in sea water, the duration of this being graduated from fifteen minutes at the beginning of treatment to two or even three hours, and to the exposure of the body to the sun which necessarily accompanies the bath. In a few specially selected cases swimming, rowing, surf bathing, and hot sea-water baths should be ordered in addition. By this method of treatment Bossi believes, as a result of many years' experience as director of a large gynecological clinic in a Mediterranean coast city, that great improvement may be obtained in many cases of the following gynecological affections: Chronic pelvic cellulitis and parametritis, chronic adnexal inflammations hyperplastic cervicometritis, puerperal subinvolution, residual hematocele, prolapsus uteri, versions and flexions, even when accompanied with adhesions, chronic endometritis, and fibromyomata. He emphasizes the fact, however, that the treatment should always be directed by a physician in accordance with the needs of the individual patient, and the local conditions prevailing at the resort at which the cure is being taken.

After-results of Appendectomy.—König (*Med. Klinik*, 1911, vii, 875) believes that in most cases persistent trouble after appendectomy or other abdominal operations is due to the formation of adhesions. He believes that certain individuals have a much greater tendency to the formation of adhesions than others, but that in any case where even the finest adhesions are once formed, any operation

may increase them. Since adhesions may form during any attack of appendicitis, the only sure way to avoid them is to remove the appendix before they have time to form; in other words, as soon as the diagnosis is made. It should be our rule to treat appendicitis as we do strangulated hernia—operate at once, do not wait for the interval. König believes that packing off the peritoneum with gauze should be avoided as much as possible, as it favors the subsequent formation of adhesions; he does not do it even in cases where the appendix is gangrenous, if no perforation is present. He lays great stress on the importance of the postoperative treatment in the prevention of adhesions. An intestine that is in motion does not form adhesions as quickly as one that is quiet, therefore he starts in on the day of operation with hot air treatments to stimulate peristalsis. A daily passage is secured by the use of glycerin enemata. The patients are encouraged to move their legs early, and are gotten out of bed as soon as possible, often on the second day after operation. In cases where adhesions already exist at the time of operation he recommends giving two tablespoonfuls of olive oil by mouth and an oil enema of 250 c.c. daily. At the end of the first week systematic abdominal massage should be begun, at first avoiding the field of operation, later, however, including the whole abdomen. He has these patients change their position in bed frequently, and assume the knee-chest posture from time to time. Very beneficial lasting results have proved the value of these methods of treatment in König's practice.

Relation Between Corpus Luteum and Breast.—Bouin and Ancel (*Presse Méd.*, 1911, No. 55, p. 577) believe that in studying the phenomenon of lactation two distinct phases must be kept in mind—(*a*) the morphological development of the glandular tissue of the breast; (*b*) the occurrence of secretory activity—these two phases being dependent upon totally separate causes. Since it has been proved by nerve sections and by transplantations that nervous reflexes cannot be considered as inciting the mammary gland to activity, we must have recourse to the theory of a chemical reflex—a hormone, developed in some distant organ, and acting on the mammary gland. In order to discover the source of this hormone, which Bouin and Ancel suspected to lie in the corpus luteum, they conducted a series of experiments on rabbits, an animal in which ovulation, and consequently corpus luteum formation, does not take place spontaneously, but occurs normally only after coitus; it may also be brought about artificially by rupturing perfectly ripe Graafian follicles with a needle or fine scissors. In this way, or by allowing coitus with male animals rendered sterile by the ligation of the vas deferens, Bouin and Ancel were able to produce in female rabbits corpora lutea without the development of pregnancy, or of any other condition which might have influenced the results. They found that following such a procedure a tremendous development of mammary gland tissue invariably took place, the acini increasing greatly in number, volume, and complexity. By about the sixteenth day this development had reached its greatest height, and from then on atrophy set in, the acini diminishing in volume, their lumina becoming obliterated, the epithelium desquamating, the ramifications growing less, and the vascularity diminishing. After a normal coitus,

followed by fecundation, on the other hand, the mammary gland continues to develop; the increase in size in the latter half of pregnancy is due, however, not to a further multiplication of cells, but to an accumulation of secretory products in the lumen of the acini; in other words, tissue growth has given place to secretory activity. It was found that in a few cases where coitus did not produce a rupture of follicles, or if all corpora lutea were destroyed by the thermocautery soon after coitus, no development of mammary tissue took place; if the destruction of the corpora lutea is done a few days later, the mammary development which has begun is at once arrested, and atrophy sets in. Bouin and Ancel believe, therefore, that the corpus luteum is the factor in producing the anatomical development of the mammary gland during pregnancy. This theory also explains the recurrent increase in size of the human breast coincident with each menstrual period, this being dependent upon the short-lived "corpus luteum menstruationis" which arises in woman as the result of *spontaneous* follicle rupture. Bouin and Ancel believe that the corpus luteum has, on the other hand, nothing to do with causing the fully developed mammary gland to begin secretory activity, but that this process is dependent upon a second hormone arising from a gland of internal secretion which they have discovered in the myometrium of the pregnant rabbit, and which they call the "myometrial gland."

Treatment of Leucorrhea.—Stocker (*Gynæcologia Helvetica*, 1911, xi, 160) calls attention to the fact that in every leucorrheic discharge are found many polymorphonuclear leukocytes. These contain a ferment having an albumin-digesting (proteolytic) action, which causes extensive liquefaction of tissue, this expressing itself as purulent secretion. It has been found that there exists in the blood serum an antiferment which fixes this proteolytic ferment. By injection of this antiferment, therefore, purulent processes can be shortened or stopped. It is necessary that the antiferment come into immediate contact with the ferment, as the action is a direct neutralization. Since 1909 Stocker has treated all cases of fluor albus on this principle, with very gratifying results. He uses "leucofermantin" (Merck), introducing a gauze strip soaked in this substance into the cervix after thorough cleansing of the latter. The gauze is changed the next day. If the uterus is much enlarged, showing that the corpus is also affected, 1 to 2 c.c. of the fluid are injected by means of a Braun's syringe under very gentle pressure into the uterine cavity. No douches are given during the treatment, in order better to control results. Of 70 patients thus treated Stocker reports 68 per cent. as being entirely cured of the discharge and the others greatly relieved.

Nasal Treatment of Dysmenorrhea.—Brettauer (*Am. Jour. Obst.*, 1911, lxiv, 215) makes a plea for the serious consideration of the nasal treatment of cases of dysmenorrhea in which no gynecological condition can be found to be responsible. In these cases the pain usually disappears within a few minutes after the application of a 20 per cent. cocaine solution to certain areas in the nasal mucous membrane which are composed of erectile tissue, and which always become swollen, hyperemic and hyperesthetic, during each menstrual period. Where the

pain is due to some uterine displacement, inflammation, or other local condition, application of cocaine to the nasal areas referred to above has no effect whatever. In those cases where it is followed by relief of pain, however, Stocker claims that a permanent cure may often be affected by cauterization or other suitable rhinological treatment, and reports four cases of severe dysmenorrhea in unmarried women who were cured by cauterization of edematous nasal mucosa, removal of spurs, enlarged turbinates, etc.

Origin and Dissemination of Renal Tuberculosis.—As the result of a series of experiments on dogs and goats, in which suspensions in sterile oil of tubercle bacilli of varying degrees of virulency were injected directly into one renal artery, Pels-Leusden (*Arch. f. klin. Chir.*, 1911, xcv, 245) believes that the theory that most cases of chronic unilateral renal tuberculosis are of hematogenic origin is correct, the infection occurring probably by means of small tissue particles, fat droplets, or other forms of emboli containing tubercle bacilli, which have passed through the lung capillaries. He believes that isolated tubercle bacilli circulating in the blood may pass through the kidney without doing any harm. In cases of severe caseous tuberculosis of the renal pelvis, with occlusion of the collecting tubules, the process may extend retrograde throughout the kidney by way of the uriniferous tubules. That tuberculosis of the kidneys can arise by retrograde transmission through the lymphatics from the lungs, pleura, or bronchial lymph glands he considers by no means demonstrated. He believes that trauma considered in its broadest sense—as an impairment of any sort of the normal integrity of the tissues—plays a certain role in the development of a local tuberculous focus, but that trauma in the sense of a direct contusion at a given point is not necessary to the development of tuberculosis at that point. As a result, however, of such a trauma, tissue particles and bacilli may be thrown off into the blood stream and then give rise to a chronic tuberculosis at some distant point.

Use of Pituiterin in Gynecology.—In cases of endometritis, metritis, and of menorrhagia due to myomata, ovarian cysts, or inflammatory conditions of the adnexa, Bab (*Münch. med. Woch.*, 1911, lviii, 1554) has seen pituiterin (hypophysis extract) produce marked results in stopping hemorrhage when hydrastis, ergot, stypticin, etc., had been used without result. He injects subcutaneously 2 to 3 c.c. once, or, if necessary, on several successive days, and has had no unpleasant after-effects except occasionally slight labor-like uterine pains. He reports that in 30 cases so treated, in many of which the bleeding had been protracted and profuse, the bleeding stopped on the first day in 33 per cent., on the second day in 36 per cent., and in only 6 per cent. was no effect whatever produced. Klotz (*Münch. med. Woch.*, 1911, lviii, 1119) reports equally favorable results from the use of the same substance in the treatment of atonic uterine hemorrhage post partum. He uses for this purpose 0.2 gm. of the gland (represented by 1 c.c. of the preparation made by Borroughs, Wellcome & Co., and by 2 c.c. of that put out by Parke, Davis & Co.), but says that the maximum dose that can be borne is unknown. He considers intramuscular injection to be the proper method of application.

DERMATOLOGY

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Pathology of Malignant Epithelial Growths of the Skin.—John A. Fordyce (*Jour. Amer. Med. Assoc.*, 1910, lv, No. 19, 1624) believes from his numerous investigations that no one agent is concerned in the malignant proliferation of epithelial tumors, and that a multiple etiology is responsible for the cutaneous carcinomata. A strong argument against the theory of the parasitic nature of the disease is the development of epitheliomata following exposure to sunlight, Röntgen rays, and other radiant energy. The action of such chemical substances as arsenic, tar, tobacco, and scarlet-red on epithelium, for which they have a special predilection, goes to show that a variety of agents have the power to stimulate epithelial mitosis which may pass into malignancy. Carcinomata which develop on scar tissue or antecedent conditions of the skin like lupus, syphilis, etc., suggest the idea of misplaced cells in some cases and in others with degenerative processes which interfere with the functional life of the cells, followed as a consequence by overgrowth of the cells.

The Tineas.—R. Sabourand, an authority, enters upon the subject of the cryptogamic disease at great length (*Brit. Jour. of Derm.*, October, 1910, pp. 334, 335), the following points being of practical interest. It is stated that different forms of fungi are responsible for ringworm and favus, and that in Paris, out of 500 cases, 150 were due to microsporon, 218 to trichophyton, and 52 to favus. Eleven species of microsporon are described by the author, 15 of Trichophyton endothrix, 15 of Trichophyton ectothrix, and 5 of favus, which affect man and certain of the lower animals. No accidents effecting the brain from the use of *x*-rays are recorded. An important practical question discussed is the danger of producing permanent loss of hair from the use of *x*-rays in the treatment of the tineas of the scalp. Sabourand takes the view that if such an accident did occur it was due to an overdose, the same region being exposed to more than one full dose at too short an interval, or to the regulation distance of 15 cm. between the anticathode and the scalp not being adhered to.

(The profession is greatly indebted to Sabourand for our present knowledge of the treatment of the tineas by *x*-rays, his labors in Paris over many years having resulted in much good for therapy.—L. A. D.)

Etiology of Elephantiasis.—G. C. Shattuck (*Boston Med. and Surg. Jour.*, clxiii, No. 19, p. 718) directs attention to the relation between edema, hyperplasia of connective tissue, and lymphatic dilatation.

The essential characteristics of the acquired form of the disease are lymphangiectasis, hyperplasia of connective tissue, and chronic edema, and these conditions may frequently be attributed to the interaction of stasis and inflammation, stases always occurring early, and persisting. Inflammation may precede or follow stasis, or may be absent at any stage of the disease, and may be acute or chronic and generally may be traced to bacterial infection. Chronic stasis or inflammation may predispose to elephantiasis, but the disease does not always result even when they occur together. Filaria is an important factor in the production of endemic elephantiasis of some countries, but is not essential to the occurrence of the endemic variety. The disease in regions where filaria abound results indirectly from filariasis through bacterial infection.

Solid Carbon Dioxide in Dermatology.—E. R. Morton (*Lancet*, August 20, 1910, p. 558) relates his experience in a large number of cases, including capillary and cavernous nevi, port-wine marks, lupus vulgaris, moles, and warts. Of capillary nevi, 212 cases were completely cured by a single application, lasting on the average forty seconds. Other cases had more applications. In cavernous nevi the results were not so successful, although 33 cases were cured by a single application, and 5 incompletely cured or not benefited. In port-wine mark every portion of the lesion had to be treated two or three times. In lupus vulgaris crusts are to be removed and firm pressure made with the crayon for at least forty seconds. The healing process occupied from two to three weeks. The results were regarded as satisfactory. In moles and warts the treatment is eminently successful. In pigmented and hairy moles from thirty to forty seconds are usually required, but the author is not sure as to the permanence of the destruction or loss of the hair due to the freezing. (But little is said about the pain following the application, which some operators find an objectionable feature of the treatment.)

Therapeutic Use of Refrigeration with Solid Carbon Dioxide.—W. A. Pusey (*Jour. Cutaneous Diseases*, July, 1910) contributes a paper of great interest in connection with this chemical agent which of late has become so popular with dermatologists for the treatment of various affections of the skin. In treating lesions up to the size of one-half inch in diameter, where the lesion is uniform in surface, one application of a mass of the snow, which is moulded or pared as nearly as possible to the size and shape of the lesion, is made. For lesions above an inch in diameter the best practice is to shape the end of the stick of CO_2 into a rectangular form in order to get perfect coaptation of the area treated. Even pressure should be exerted, in order to avoid irregularities in the freezing of the tissues. Warm or cold bathing of the part after freezing relieves the pain. As a rule, no after treatment is called for, beyond ordinary antiseptic precautions. Blebs that form may be emptied or allowed to rupture without surgical interference. Untoward effects seldom result. Scars, if these result, are usually of a benign or excellent character. The list of diseases in which this agent may be employed with the expectation of satis-

factory results is large, among which may be specially mentioned vascular nevus, especially small lesions up to the size of a coin; obstinate chronic inflammatory lesions, as lichen and thickened eczematous patches; lupus erythematosus; senile pigmentary spots of the hands and face; warts and callosities; moles and pigmentary nevi, especially small nevi. For the ordinary forms of cutaneous carcinoma the author prefers other methods of treatment. (The paper is an interesting and valuable contribution to cutaneous therapeusis.—L. A. D.)

Our Knowledge of Pigment Production.—J. E. R. McDonagh (*Brit. Jour. of Derm.*, October, 1910) gives a summary of the discoveries made since the observations of Koelliker in 1860, who found in the epidermis of a fish pigment cells which sent their processes into the corium. Many of these branched cells being found in the corium, he concluded that they originated in the corium. Kebert after him regarded these "chromatophores" (as Koelliker called them) as connective tissue cells which had the power of manufacturing pigment for the supply of the epidermis. Riehl (in 1884) called these pigment cells "wander cells," and because he found them mostly arranged around the bloodvessels of the corium, presumed they built up or derived their pigment from the blood and carried it to the epidermis. Ehrmann in part confirmed Riehl's studies, but stated that the wander cells stop short when they reach the epidermis, the further progress of the pigment being performed by an intermediary cell branched and ameboid in character, and epithelial. Karg transplanted by grafts negro's skin on white skin, and vice versa. The former became white and the latter black, showing that the cells in the corium were the cause of the pigmentation. Ritterer (in 1887) and others since have shown that epidermic pigment had an autochthonous origin. Meirowsky's important recent experiments with the Finsen rays show that pigment was found in the epidermis only, and the origin of pigment is autochthonous. Hemoglobin plays some part in the production of pigment, but is not the source of all. It is impossible to determine the relation blood bears to pigment. It would seem that the production of pigment may be regarded as a metabolic process, affecting the proteid molecule of the cell, this metabolic change being due to the action of a ferment; the studies by several observers in recent years favoring the part played by a ferment, especially that named by Bourquelot "tyrosinase." The further connection between pigment and metabolism is shown in ochronosis, where the cartilage of the body becomes black.

X-ray Therapeutics in Dermatology.—The following is condensed from a lengthy review of a book (just published) by Frank Schultz, by "J. B. L.," in the *British Journal of Dermatology*, for October, 1910. Dr. Schultz is chief of the Light Department at the Berlin Kgl. University Polyclinic, the work being based on an experience with 25,000 *x*-ray applications. It is stated that the two extreme results of the action of *x*-rays are surprising cures and serious injury. The exclusion of unsuitable cases and avoiding all injurious after effects in cases treated is the duty of every *x*-ray therapeutist. The question of idiosyncrasy, or undue capacity of reaction to *x*-rays, is

of great importance from a forensic as well as a therapeutic standpoint. Cases of general reaction are recorded in literature, and also eruptions resembling toxic erythemata (with or without fever), following the treatment of circumscribed, as well as more extended, areas, by *x*-rays. Holzknecht believes that toxic erythemata only follows burns, and are due to absorption of *x*-rays necrosed products. They cannot, therefore, be regarded as cases of idiosyncrasy, and apart from such burns Schultz met with no such reaction in his large experience. Hypersensibility to *x*-rays may vary in the same patient at different times, and hence from a legal standpoint the general question of idiosyncrasy is not so important as the question of the exact dosage employed in a given case. At the Radio-therapeutic Institute, in Berlin, every dose is entered in a record book, and is only administered in the presence of a physician, though it is doubtful if the physician must necessarily be present in the apartment during the entire period of the *x*-ray application, if he personally sees that the current is stopped at the right time. Schultz has not found much benefit from *x*-rays in acne rosacea. He does not employ it in tinea kerion. In sycosis vulgaris good results often follow $\frac{1}{3}$ dose, and cases rebellious to this treatment often improve under combined *x*-ray and high-frequency (unipolar) applications. The treatment of hypertrichosis by *x*-rays was not found satisfactory, inasmuch as, if carried far enough to cure the local growth, atrophic changes in the skin and other grave dangers occur. Hyperidrosis seems benefited in some cases, especially under full doses, but other cases show no improvement, and it is difficult or impossible to determine beforehand which type of case clinically is likely to be benefited. Schultz thinks that the damage to growing bones has obtained undue prominence from the experiments upon animals, for he has not met with such cases.

Neuralgia Paresthetica.—S. Sherwell (*Jour of Cutaneous Diseases*, June, 1910), gives his experience with a case of this disease, which was fully described in 1906, by Dr. J. C. White, of Boston. The region affected, as, for example, a limb, becomes the seat of a variety of perverted sensations, such as tingling, tenseness, or still more acute superficial tearing, darting pain, with numbing of sensation. It may begin with a glowing sensation, or like the beginning of herpes zoster, and in the author's belief the pains are caused by the same mechanical means, namely, pressure on a nerve and its continuity; but it is a disease of sensory disturbance only, at least in his cases, though Dr. White found some objective symptoms. He concludes that the condition arises from a constriction or pinching of a nerve as it passes through tough fascia, irritation resulting therefrom. Rest and massage produce temporary relief, though not a cure. (In which case the use of heat and cold or friction or massage produced no relief whatever.)

Sporotrichosis in Man.—From the pen of the late and distinguished James Nevins Hyde, of Chicago, conjointly with D. J. Davis (*Journal of Cutaneous Diseases*, July, 1910), comes a valuable article on this comparatively new and but little known disease affecting both man and some of the lower animals, notably the horse ("mycotic lymphangitis in horses"). Experiments upon animals and bacteriological

studies are given and pictured, rendering the lengthy article a valued contribution to medicine. A synopsis of the conclusions of the authors may be given. The type of the dozen or more instances of sporotrichosis in man observed in America practically corresponds with that observed in France and elsewhere in Europe, the disease being due to the organism first described by Schenck, and properly named by Hektoen the Sporotrichium Schenkii. Some of the American cases of mycotic lymphangitis, or epizoötic lymphangitis, in horses are due to the presence of this growth, and should be described as instances of sporotrichosis.

Effect of Radium on the Skin.—Guyot (*Journal of Cutaneous Diseases*, May, 1910, p. 269) gives a lengthy article, with experiments on the subject, in *Archiv. f. Derm. u. Syph.*, 1909, from which the following practical points may be abstracted. In the first two weeks desquamation appears, and in the third week loss of epidermis and hair, followed by ulceration or progressive atrophy of the skin. In the corium there is cellular proliferation and hyperplasia of connective tissue, but the hair papillæ, elastic tissue, and muscles remain unaffected. The blood and lymph vessels are dilated, but no change occurs in their walls. It may be said that radium acts as a physical and chemical irritant, different effects following different periods of exposure, and that reparative changes are slow.

The Skin Atrophies.—Finger (*Brit. Jour. of Derm.*, June, 1910, p. 202) divides all atrophies of the skin into two groups: (1) Firm atrophy, as observed in the last stages of lupus erythematosus and scleroderma, this being found to be reduced in size, thinned, fixed firmly to the underlying strictures, stretched, smooth, shiny, and only with difficulty raised into folds. This is seen especially in scleroderma. (2) In other cases the skin is loose. In cross-section it is also much reduced in size, but is not adherent to the underlying strictures, lying loose, consequently in wrinkles, therefore easily raised and thrown into folds. The latter group include cases like the well-known and depicted one of Buckwald. Pick's "erythromelia" and Neumann's "erythema paralyticum" are undoubtedly commencing stages of idiopathic atrophy, and Herxheimer and Hartmann's cases of "acrodermatitis chronica atrophicans." Finger then goes on to describe other described and recognized clinical forms of atrophy. (There exist a number of beautifully executed wax models of various forms of atrophy of the skin which the abstractor has recently viewed in Professor Finger's museum.—L. A. D.)

Molluscum Contagiosum.—Norman Walker (*Brit. Jour. of Derm.*, September, 1910) enters into the question of the distribution of this disease of the skin, his experience and studies not being in accord with those of Graham Little, who believed there was a connection between the disease and seaports. Walker is much more inclined to the view that public baths are a means of its spread, and refers to the experience of physicians in Damascus, where it was known locally by an Arabic name which meant "the itch of the bath." The field of Dr. Walker's observation was Edinburgh, where the disease seems

to be frequent, 45 cases having been observed in two and one-half years. (In Philadelphia the disease, beyond an occasion of epidemic in a children's asylum, is not only rare, but ill-developed as to the individual lesions, most of them being small and imperfectly formed. —L. A. D.)

Dermatitis Exfoliativa Treated with Quinine.—W. H. Mook (*Journal of Cutaneous Diseases*, September, 1910) directs attention to the value of quinine in full doses in this well-known, but uncommon, disease. A case is reported in which it succeeded in effecting a cure on two occasions, five-grain capsules of the hydrochlorate (preferred to the sulphate), four or five times daily, being prescribed. The author had previously reported 6 cases successfully treated by the same method. No local treatment was used. (It is questionable if cases, such as the one here reported, should not rather be diagnosticated and designated as pityriasis rubra than dermatitis exfoliativa. But irrespective of this point, the therapeutic note given is distinctly valuable.—L. A. D.)

Eucarin, a New Emollient.—G. H. Jackson (*Journal of Cutaneous Diseases*, June, 1910, p. 294) reports favorably of this new medicament emanating from Dr. Unna, of Hamburg. It is made of vaseline, acted upon by a substance obtained from wool-fat, which it is claimed takes up a large amount of water, and is in consequence a very cooling ointment. Unna found it useful in ichthyosis, and Jackson, excellent for various forms of cutaneous disease in which the skin was dry. Thus it is useful in chapped hands and similar conditions of the skin. He usually combined it with cold cream ointment, about ℥iij to ℥j, which proportions make a desirable ointment. It is useful upon the scalp in cases where a distinctly greasy application is not desired. It does not become rancid.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Cultivation of the Leprosy Bacillus.—Clegg (*Philippine Journal of Science*, 1909, iv, 77 to 79, 403 to 415) based this work upon the assumption that the leprosy bacillus derives its nutrition from the products of the tissue cells and the cells of the lesions in which it is encountered. Since this bacillus occurs so frequently within the protoplasm of these cells, a unicellular organism was selected which could be cultivated and which corresponded in a degree to the living tissue cells; that is, an organism which contained both nucleus and protoplasm. The amœba is readily grown upon artificial culture media and further

fulfils the other requirements. The method for obtaining cultures of the leprosy bacillus was essentially as follows: The amœba were isolated from water by adding 1 c.c. of alkaline bouillon to every 100 c.c. of the water in question. After twenty-four to forty-eight hours the surface was examined and if the amœbæ were present a loopful of the surface water containing the amœbæ was transferred to the surface of agar in a Petri dish which had been previously inoculated with cholera vibrios. The amœba-cholera culture was then transferred to the surface of agar slants and after twenty-four hours inoculated with the suspension of leprosy material. These slants were incubated for seven days at body temperature, and the growth transferred weekly to fresh slants. At the end of from four to six weeks, acid-fast organisms were obtained in pure culture by heating the "pure-mixed" culture of the cholera amœba-leprosy to 60° C. for 30 minutes. The acid-fast organisms survived this heating, while the amœba and cholera vibrios were killed. These acid-fast organisms grew readily when transplanted to plain agar and other media. The organisms stained in a characteristic manner by the Ziehl-Nielson method. In order to prove that these organisms were not tubercle bacilli, considerable amounts of the pure culture were inoculated subcutaneously into guinea-pigs. A week later an indurated nodular thickening appeared at the site of inoculation in some of the guinea-pigs. In four weeks the lesions spread over the abdominal walls, the hair over the lesions fell out, the animals became emaciated, and death occurred between four and five weeks after inoculation. Cultures from these guinea-pigs were negative. The smears showed large numbers of acid-fast bacilli, the majority of which were intracellular. Three more guinea-pigs were inoculated in a similar manner and with similar results. The organisms were found not to be tubercle bacilli. In one set of experiments the organisms were carried from pig to pig for three successive transfers. In only one instance was it possible, however, to reclaim the acid-fast organism by growing it in symbiosis with the amœba-cholera culture. Several monkeys were inoculated, all of which proved refractory. The guinea-pigs which were inoculated subcutaneously with a pure culture of the acid-fast organism developed lesions in some instances at the site of inoculation, which bore a certain resemblance to the leprous lesions of man both macroscopically and microscopically. The organisms were short, plump, acid-fast bacilli, occurring mostly in clumps. They grew readily, although slowly, in media which was 1 per cent. alkaline in phenolphthalein. It was noticed that repeated inoculations were necessary to obtain growths. These results were soon corroborated at the Leprosy Investigation Station of the United States Public Health and Marine Hospital Service at Honolulu, H. I.

Currie, Brinkerhoff, and Holman (*Public Health Reports*, 1910, xxv, No. 34) repeated Clegg's work on the cultivation of the leprosy bacillus and have also succeeded in obtaining growths of acid-fast organisms upon artificial media. These investigators pointed out additional factors which are not mentioned in Clegg's article and which are necessary to insure successful results. The amœbæ must be active in order to obtain a pure symbiotic culture with the cholera vibrio. The agar slants must have a slight excess of condensation water, since the long period of incubation results in a considerable desiccation of the

media. Before adding the leprosy material to the amœba-cholera culture the workers at Honolulu found that it was desirable to keep the amœba-cholera culture at 37° C. for five days in order to encourage the encystment of the amœbæ. Under these conditions the amœba were found to be far less phagocytic, and this inhibition of phagocytosis appears to be essential in order to prevent the digestion of the leprosy bacilli. Along somewhat similar lines, but with slightly modified technique, Duval, of New Orleans also obtained an acid-fast bacillus in pure cultures from leprosy material.

Duval (*Jour. Exper. Med.*, 1910, xii, 649 to 665) cultivated an acid-fast bacillus by growing it in a symbiotic culture of the amœba and typhoid bacillus. The agar was alkaline to the extent of 1 per cent., and the amœba-typhoid culture was grown at room temperature for forty-eight hours before the introduction of the leprosy material. After the acid-fast organisms had grown the typhoid bacillus was killed by a strong bacteriolytic serum and it was found that under these conditions the leprosy bacillus grew in symbiosis with the amœbæ. It was not possible to obtain growths of the leprosy bacillus in symbiosis with the typhoid bacillus alone. The amœba appears to be the essential factor. Duval also tried a medium containing tryptophan, cystin, and leucin (1 per cent. of each). His idea was to supply food for the leprosy bacilli analogous to that of the tissues. He used this medium on the surface of banana slants in order to promote oxidation. Agar slants were similarly treated with these substances and the amœba-leprosy culture grew both on the banana slants and agar slants under these conditions. According to Duval the optimum temperature of growth for the leprosy bacillus in artificial media appears to be between 32° and 35° C., and the presence of light is an important feature. The organisms thus obtained grew in subcultures and were acid-fast. They were proved not to be tubercle bacilli by inoculation experiments in guinea-pigs and rabbits. Inoculation experiments were successful in Japanese dancing mice. The earliest macroscopic changes appeared after four weeks as discreet glistening nodules, $\frac{1}{3}$ mm. in diameter, and firmly attached to the serous surface of the peritoneal organs. Histological structures were the same as those in human lesions. Inoculations into the mice both with artificially cultivated organisms and from human cases of leprosy were successful, and it would appear that this successful direct inoculation helps to establish the identity of the organism in the artificial cultures. Duval's work differs in one respect materially from that of Clegg as well as Currie, Brinckerhoff, and Holman in that he found that his organisms grew best at 32° to 35° C., and that body temperature seriously inhibited or even prevented their growth. The other investigators, on the contrary, were always successful in obtaining growths at 37°. As the leprosy bacillus grows well in the human tissues, we would expect *a priori* that 37° C. would be its optimum temperature under conditions of artificial cultivation. The cultivation of the bacillus of leprosy has long been a stumbling block to the bacteriologist, but it now appears that we have at last the true solution of this crux. Of the hundreds of attempts to grow this organism in the past, that of Weil of the Pasteur Institute deserves special mention. He obtained one colony of an acid-fast organism upon rabbits' serum.

Chemo-immunological Studies on Localized Infections.—In spite of a large amount of experimental work upon pneumococcus infections it is not at all clear as to the manner in which the body protects itself against local infections of the pneumococcus. Antipneumococcus serum, it is known, has agglutinative properties, but no lytic action upon the pneumococcus. The serum, however, contains opsonins which further to a certain extent phagocytosis of pneumococci by leukocytes. Under ordinary circumstances the facility with which pneumococci are taken up by leukocytes varies greatly, the virulent strains being almost insusceptible of phagocytosis. Lamar (*Journal of Experimental Medicine*, 1910, xiii, 1) has found that highly dilute solutions of alkaline oleates which do not suffice to alter the morphology or reproductive power of pneumococci, nevertheless produce profound changes in their structure; for pneumococci treated with sodium oleate not only become more subject to autolysis, but become subject to lysis by blood serum. The lysis is more marked when immune serum is used. It is necessary, however, that the sodium oleate should act upon the pneumococci in the test-tube before serum is added, since the serum protein contains a substance inhibiting the action of sodium oleate. It was found that boric acid in proper amount would prevent the inhibitive action of serum against sodium oleate. A mixture, therefore, of sodium oleate, boric acid, and serum was capable of killing pneumococci in vitro and preventing the infection of a susceptible animal from the injection of a lethal dose of pneumococci. And infection can not only be prevented when the mixture of immune serum, soap, and boric acid is added to the pneumococci before injection into the peritoneal cavity of small animals, but the infection can likewise be prevented when a therapeutic injection of a mixture of these three substances mentioned is made to follow the inoculation of highly virulent diplococci. Though the virulence of the pneumococci is somewhat diminished by soap treatment, the treated organisms are not rendered more susceptible to phagocytosis. It would appear that the action of soap is exerted upon the lipoidal moiety of the bacterial cells through which they are rendered more susceptible of destruction by serum. The experiments which have just been described represent a manner of disposing of pneumococci which in all probability takes place in a resolving pneumonic exudate, the autolyzing leukocytes furnishing the chemical substance which brings the pneumococci under the deleterious influence of body fluids.

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ORIGINAL ARTICLES

TRICUSPID STENOSIS, WITH A REPORT OF FIVE CASES.[1]

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A search of the literature reveals two facts concerning tricuspid stenosis. First, the lesion is comparatively rare; and second, very few cases are recognized during life. Up to 1908, 187 cases had been reported, and in only 12 has a correct *intra vitam* diagnosis been made. Of 26,000 medical admissions to the Johns Hopkins Hospital, there have only been 8 cases in which there was either a clinical or postmortem diagnosis of tricuspid stenosis. In only 5 cases has the lesion been found post mortem out of a total of 3500 autopsies. In only 1 of these 5 cases (Case I) was a correct diagnosis made during life. Including the cases here reported, there have been only 13 out of a total of 195 cases in the literature in which the lesion was recognized.

Case I (Med. No. 24,057).—*Diagnosis of combined tricuspid, mitral and aortic stenosis made during life; confirmed at autopsy. The generalized narrowing of the whole aorta would suggest the possibility of a congenital element in the production of the stenosis. The tricuspid orifice was almost obliterated, the measurements of the slit being 1 cm. in length and 4 mm. in width. No rheumatic history.*

A. J., female, married, aged thirty-seven years, was admitted to the private ward of the Johns Hopkins Hospital, April 30, 1909, complaining of shortness of breath and dropsy. The writer had

[1] Read before the Association of American Physicians, May 10, 1911.

seen the patient the day previously with Dr. H. Warren Buckler, at Dr. Kelly's Sanitarium, where she had been sent for suspected pelvic trouble. As no gynecological disease was found, and since it was perfectly obvious that there was serious organic heart trouble, she was transferred to the Johns Hopkins Hospital.

The family history was unimportant. She had not been a "blue baby." Her husband stated that she had possessed a "high color" even before they were married seventeen years ago. She had never had any inflammatory rheumatism or arthralgia. There had been recurring sore throats. At the age of nineteen she was seriously ill for several weeks with severe abdominal pain and constipation. Neither she nor her husband knew the true nature of this trouble.

The symptoms for which she was admitted had begun nineteen years before with shortness of breath. After an attack of influenza, twelve years ago, she became worse. The dyspnea, palpitation of the heart, and cyanosis had been present since then, and the cyanosis had been especially marked for five years. In 1904 she had an attack of broken compensation, with edema of the feet, and it was then recognized by the family physician that she had heart disease. Since that date there have been two attacks of decompensation, the last one beginning eight weeks ago. Orthopnea first manifested itself during this attack. Swelling of the legs and abdomen have been marked. The cyanosis had been extreme recently.

On May 1 the writer dictated a note from which the following abstract is made: The patient was of short stature and rather stout. Very extreme cyanosis of the ears, lips, cheeks, and fingernails. There was a distinct icteroid tint of the face and sclerotics. It was impossible to count the radial pulse, only an occasional beat being perceptible. On auscultation over the heart, there were 79 beats per minute.

The examination of the lungs revealed a large pleuritic exudate on the left side and some dulness at the right base, with numerous medium moist rales on inspiration.

The note on the heart was as follows: "The point of maximum cardiac impulse is just seen and felt in the fifth interspace, 11 cm. from the midsternal line, and just in the midclavicular line. There is very slight precordial bulging, but practically no pulsation or heaving. Systolic shock distinctly tapping at the apex. No definite thrill. The deep cardiac dulness begins at the upper border of the third rib at the left sternal margin, and extends from a point in the fourth right interspace, 5 cm. from the midsternal line and merges in the flatness due to the pleural fluid on the left side, but apparently it extends considerably beyond the mammillary line. There is apparently no Rotch's sign to the right. The absolute cardiac dulness begins at the upper border of the fourth rib at the left sternal margin, and reaches from the right sternal mar-

gin, at the level of the fourth rib, to the point of maximum impulse in the fifth interspace. On auscultation, the first sound is very snapping at the apex. There is, at present, no definite presystolic murmur, but there is a slight echoing, rumbling murmur in diastole. There is no systolic bruit at the apex. The second sound is not audible here. The heart's action is quite irregular. In the fourth and fifth interspaces at the left sternal border the snapping quality of the first sound is even more marked than at the apex, and the tapping systolic shock is very striking here. The second sound is here audible and is definitely reduplicated. There is no rumbling presystolic murmur in the tricuspid area. In diastole, there is, however, on very careful auscultation, a very faint, soft, prolonged, blowing diastolic murmur. At the aortic area yesterday there was a faintly palpable systolic thrill. It is just perceptible this morning. The first sound is audible, and is accompanied by a very rough systolic murmur, transmitted upward to the sternoclavicular articulation. The second aortic is quite loud, and, if anything, accentuated. There is no aortic diastolic bruit heard here. Pulmonic sounds clear. Second pulmonic accentuated. The external jugulars are only slightly distended."

The liver flatness extended from the sixth rib to a point apparently on a level with the costal margin in the mammillary line. In the median line it reached only to the tip of the ensiform. Owing to the edematous abdominal walls, it was not possible to satisfactorily palpate for the liver border. There was no visible or palpable liver pulsation. There was thought to be a moderate amount of ascitic exudate.

There was very marked edema of the dependent portions of the trunk, as well as of the hands, arms, thighs, and legs. Over the backs of both wrists, there were quite numerous pin-point and pinhead sized petechiæ.

On the previous day, April 30, Dr. Boggs had heard a mitral systolic murmur at the apex, and a faint aortic diastolic murmur down the left sternal border. Dr. Henry, the house officer, had noted a definite rumbling murmur in diastole at the mitral area, and that the liver border extended half way to the umbilicus. It was also noted that there was no systolic pulsation of the veins of the neck.

During May 1, the patient's condition gradually became worse. The removal of 500 c.c. of straw-colored fluid from the left pleural sac failed to give much relief to the dyspnea. There was a curious sighing dyspnea, the respirations being only twelve to the minute. The heart was even feebler, and the rate had risen to 120 per minute.

On May 3 she was much worse. Only 200 c.c. of urine had been secreted into the bladder since mid-day of May 2. The heart action became even feebler, and more irregular, and the rate had risen to 140 beats per minute. The cardiac murmurs had practically dis-

appeared. The respirations became extraordinarily slow, and the patient died at 3.15 P.M.

Clinical Diagnosis. Intra vitam, a diagnosis of mitral stenosis and insufficiency, aortic stenosis and insufficiency, and a probable tricuspid stenosis was made.

Autopsy Report (*No.* 3214). The autopsy was performed by Dr. W. C. MacCullum.

Anatomical Diagnosis. Tricuspid, mitral, and aortic stenosis; dilatation and hypertrophy of the auricles; contraction and atrophy of the ventricles; chronic passive congestion of all tissues except lungs—extremely marked in liver—less so in other organs; generalized edema; pleural and pericardial effusion; compression, atelectasis, and edema of the lungs; hemorrhagic infarction of the lungs; acute diphtheritic, hemorrhagic colitis; generalized narrowing of the arteries and thickening of the veins.

I quote the following from Dr. MacCallum's report: The body is that of a slenderly built white woman, 167 cm. in length. There is marked edema of the legs, genitalia, and to a less extent of the abdomen, hands, and arms. There are petechiæ over the hands and arms, and pigmented areas over the legs. There are marks of needles through which the edematous fluid was drawn. The subcutaneous fat is present in moderate amounts, yellowish red in color. This is true also of the very much congested fat in the omentum and the mesentery. The peritoneal cavity contains no excess of fluid. The serous surfaces are everywhere congested. The liver is very rough and nodular, and extends 8 cm. below the ensiform, and 4 cm. below the costal margin. It is very deep blue in color, and on pressure the blue color disappears and leaves a pale brown liver substance. A considerable quantity of fluid is present in each pleural cavity, perhaps 600 c.c. in the left and not so much in the right pleural cavity. The left lung is markedly compressed and bound by a few adhesions at its anterior part. Compression of the right lung is not so marked.

The *pericardium* is distended with clear straw-colored fluid (400 c.c.). There are distinct remnants of thymus tissues. The heart is not especially enlarged throughout. The right auricle is enormously distended, however, and from the insertion of the inferior cava to that of the superior cava measures about 7 cm. Its surface shows a number of tendinous patches. It is very irregular, distorted, and retracted here and there. The fat about the right ventricle is congested. The left ventricle is firmly contracted. The veins and arteries are prominent over its surface. It is deep blue in color. The left auricle is small and apparently nearly empty. The dilatation, therefore, is especially on the right side of the heart and particularly in the right auricle.

Heart. Weight, 300 grams. The heart superficially is smooth, except for the presence of the tendinous patches described, which are

found especially over the right side. The right auricle contains only fluid blood, except in the auricular appendage, where there is a globular thrombus about 1.5 cm. in diameter, the surface of which shows the corrugations very distinctly. This projects from the intertrabecular space. It contains some soft, semifluid, brownish, bloody material, and a central portion, which is rather firmer. On opening the right auricle, it is found that the auricular walls are distinctly thickened. This is especially true of the great trabeculæ which run across its walls. Among the trabeculæ at one point in the auricular appendage there is a small globular thrombus which has a corrugated surface, and which is internally softened. It measures about 1.5 cm. in diameter. The tricuspid orifice is almost obliterated. The valves stretch across the ring and form a wrinkled diaphragmatic membrane, which is thicker in some parts than in others. They leave a small orifice about 1 cm. in length, and about 4 mm. in diameter, which is slightly irregular and bordered by a rough, thick margin. This is the only passage for blood into the right ventricle. The coronary sinus is enormously widened. It easily admits the gloved thumb. The right ventricle is diminished in size. Its wall is about 5 mm. in thickness. Its length is only about 5.5 cm. The papillary muscles and the chordæ tendineæ are extremely thickened. The pulmonary orifice measures 6.5 cm. in circumference. Its valves are perfectly delicate and normal in form. The pulmonary artery is smooth and delicate. The endocardium of the left auricle is unusually thickened and opaque. The wall of the left auricle is somewhat thickened, measuring at its maximum 5 mm., on an average about 2 or 3 mm. The mitral orifice is markedly contracted. The mitral valves are extremely thick, and are grown together so as to form the usual type of diaphragm which one finds in cases of mitral stenosis. The orifice itself is crescentic, measuring about 2.5 cm. in transverse diameter and only about 4 mm. across. At one end it has the appearance of being split or torn and is covered with a slight roughening, which looks somewhat like a minute thrombus mass. There are no thrombi in the left auricle. The left ventricle is small. It measures about 7 cm. in length at its maximum, and averages about 14 mm. in thickness. It is apparently not at all hypertrophied. The conus arteriosus of the aorta is somewhat constricted by the growth of fibrous tissue. The valvular orifice is very small, measuring only about 1 cm. in length, and 5 or 6 mm. in breadth. The aortic valves are enormously thickened and grown together, so that the circumference of the valvular orifice is only 3.5 cm. The sinuses of Valsalva are largely hollowed out. The valves at their junctures are grown together throughout more than one-half of their length, and in this way, there is a thick, triangular mass formed at the junction of each two valves. The sinuses of Valsalva are not very completely separated from one another on account of the retraction of the

intervening projection. On the ventricular side of this valvular ring, there is at one point, a cavity in one of these triangular masses, in which the tissue has become blackened and discolored. This blackening shines through a superficial layer of white tissue, but at one point there has occurred a break into the substance of this mass, and a soft, brownish material has poured out through the orifice. The orifice is about 6 mm. in length and 2 mm. in breadth. The aorta just at the valves measures about 5 cm. in circumference. It widens a little above the valve, where it measures about 6 cm. in circumference. Its surface is fairly smooth, but there are a few small sclerotic plaques. The coronary orifices come off a little above the aortic valves. The coronaries are distinctly sclerotic, but there is no actual occlusion. The *aorta* is somewhat narrowed, and measures only about 3.5 cm. in circumference. In the lower portion just above the bifurcation, it measures only 2.5 cm. in circumference. It is especially sclerotic in its lower portion, but there is some sclerosis throughout. The inferior vena cava is, on the contrary, rather wide, and its wall is distinctly thickened, so as to become opaque and white. The carotids and other arteries coming off from the arch appear distinctly smaller than normal.

Liver. Measures 19.5 by 16 by 6 cm.; weight, 1100 grams. Its surface is extremely irregular. After an amount of blood has run away, it is much bile stained. There are large projecting nodules upon the upper surface. Particularly the left lobe shows a very nodular appearance. The inferior cava, as it passes through the liver, is especially thickened and roughened. The gall-bladder contains very thick, dark bile. The lower surface of the liver is also extremely irregular in form. On section, the liver presents an extraordinary appearance. There is absolutely none of the original lobulation to be made out, but there has evidently been great destruction of the lobules in portions of the liver, remnants of which are left; while in other areas there are large radiating lobules which are enormously larger than the original ones. The whole liver has a greenish, bile-stained appearance, and is remarkably variegated by the alternation of these large succulent areas which have a pale, grayish-green color, and a smaller scarred or hemorrhagic area. In some parts, especially the upper part of the right lobe, there are areas almost entirely composed of fibrous tissue, in which the liver substance seems to have been very largely destroyed.

In this case, the diagnosis of mitral stenosis and insufficiency, and of aortic stenosis and insufficiency, were made from some of the usual physical signs of these lesions which were present. We did not feel, however, that these lesions were sufficient to account for all the patient's symptoms. Our reasons for concluding that there was an associated tricuspid stenosis were as follows: (1) The extreme cyanosis. (2) The considerable increase in the cardiac dulness to the right of the sternum. (3) In spite of the fact that

there was an exaggerated systolic shock and a snapping first sound at the apex, both these physical signs were even more striking in the fourth and fifth interspaces at the left sternal margin. The absence of any presystolic thrill or rumbling murmur at the tricuspid area was probably due to the final weakening of the contractions of the left auricle which had become so enormously dilated. This case demonstrated the value of the exaggerated systolic shock and the snapping quality of the first sound at the tricuspid area in aiding in the diagnosis of tricuspid stenosis, just as they are of great importance in the diagnosis of mitral stenosis. In the latter lesion they are often present without either the presystolic thrill or murmur. The tricuspid narrowing in this case was extreme, the measurements of the opening being 1 cm. in length by 4 mm. in width. Whereas, the narrowing of all three orifices was probably endocarditic in origin, yet the possibility of a congenital origin must be seriously considered. This was suggested by the marked hypoplasia of the aorta.

The remaining 4 cases will be reported very briefly, although some of them developed remarkable complications which might be dwelt upon.

Case II (Med. No. 9423).—E. O'H, female, white, single, aged thirty-five years, was admitted to the hospital January 4, 1899. She remained continuously in the hospital until her death on October 22, 1902. She had chorea at eleven, and there had been eight attacks of acute articular rheumatism before admission. She had been dyspneic and slightly cyanotic for years. She had characteristic signs of mitral stenosis, but at no time was a tricuspid stenosis or aortic lesion suspected. During her observation in the hospital, she had an embolism of the left popliteal artery, as well as a thrombosis of the left external jugular and subclavian veins. Death was preceded by the sudden development of symptoms and signs of thrombosis of the aorta with complete loss of power of both lower extremities and anesthesia to the waist-line.

Autopsy No. 2015 (Dr. MacCallum). *Anatomical Diagnosis.* Chronic endocarditis; stenosis and insufficiency of the tricuspid and mitral valves; contraction of the aortic valves; occlusion of the left jugular and subclavian veins with subsequent canalization; thrombosis of the aorta and both common iliacs; infarction of the spleen and kidneys; chronic passive congestion of the viscera; obesity.

The right auricle was tremendously enlarged, and the tricuspid orifice was represented by a slit measuring 2 by 1 cm.

Case III (Med. No. 14,415).—I. K., female, white, married, aged thirty-five years, was admitted to the hospital May 28, 1902, complaining of dropsy. She had never had chorea, rheumatism, nor recurring tonsillitis. The cardiac symptoms began seven years before admission, with dyspnea and edema of the legs, during the latter

months of a pregnancy. These symptoms had continued up to the time of admission.

The patient was markedly cyanotic and dyspneic. The pulse was of very small volume and irregular in force and rhythm. The heart was much enlarged to the left, but there was no enlargement to the right, as made out by percussion. There were characteristic auscultatory signs of mitral stenosis and insufficiency and of tricuspid and aortic insufficiency. There was nothing in the records to indicate that either tricuspid or aortic stenosis were suspected.

Autopsy No. 1937 (Dr. MacCallum). *Anatomical Diagnosis.* Chronic endocarditis; aortic, mitral, and tricuspid stenosis and insufficiency. Chronic passive congestion of the viscera. Hemorrhagic infarction of the right lung. Serofibrinous pleurisy with compression of the lung. Chronic endometritis.

The tricuspid orifice was not narrowed to the same degree in this case as in the previous two cases. It admitted only two fingers however.

Case IV (Med. No. 14,525).—A. B., female, white, single, aged thirty-six, was admitted to the hospital, June 27, 1902, and died the following day. She had an attack of rheumatism as a child and said she had suffered from heart trouble ever since she was a schoolgirl.

The patient was desperately ill on admission. There was extreme cyanosis and marked dyspnea. The heart was in delerium cordis, and very little could be made out. There was a presystolic thrill at the apex, together with a systolic and presystolic murmur. Apparently no suspicion of a tricuspid stenosis was entertained.

Autopsy No. 1957 (Dr. Opie). *Anatomical Diagnosis.* Chronic endocarditis of mitral valve with stenosis. Chronic endocarditis of tricuspid valve with fusion of segments and stenosis. Dilatation and hypertrophy of the right side of the heart. Chronic passive congestion of lungs, liver, spleen, and gastro-intestinal tract. Myoma of uterus.

The right auricle was greatly distended and formed about one-third of the anterior surface of the heart. There was a marked degree of narrowing of the tricuspid orifice, two of the segments being completely welded together.

Case V (Med. No. 17,934).—M. W., female, white, married, aged twenty-nine years, was admitted to the hospital December 27, 1904. Death occurred the following day. When twenty years of age a physician had told her that she had heart disease. There was a history of rheumatism. She had never had dyspnea or edema before May, 1904.

There was extreme cyanosis and marked increase in the cardiac dulness toward the right. There were auscultatory signs of mitral stenosis and insufficiency, aortic insufficiency, and tricuspid insuffi-

ciency. There apparently was no suspicion of the existence of tricuspid stenosis.

Autopsy No. 2449 (Dr. Bunting.). *Anatomical Diagnosis.* Chronic endocarditis of the tricuspid, mitral, and aortic valves, with stenosis of the tricuspid and mitral orifices; hypertrophy and dilatation of the heart; thrombosis of the right auricular appendage, with a free thrombus in the left auricle; general chronic passive congestion of the viscera; red atrophy of the liver; general edema with ascites; infarction of the kidneys.

The contraction of the tricuspid orifice was moderate. It admitted the tips of two fingers. The statement regarding the aortic orifice was as follows: "The segments of the aortic orifice are thickened and curled and apparently would present a slight interference to the outflow of blood, although the orifice admits the tip of the index finger."

We may briefly summarize these 5 cases as follows: All were females. Their respective ages were thirty-seven, thirty-five, thirty-five, thirty-six, and twenty-nine years. There was a definite history of rheumatism in 3, one of these also having chorea. The etiological factors were not clear in the other two. It is possible that there may have been a congenital element in Case I. In all 5, there was a marked mitral stenosis lesion. In 3 of the 5 there was a definite aortic stenosis. In the fourth there was thought to be some aortic narrowing. In the fifth case the aortic valves were normal. In all 5 the pulmonic valves were unaffected.

Duroziez,[2] in 1868, Leudet,[3] in 1888, J. B. Herrick,[4] in 1897, and W. W. Herrick,[5] in 1908, have anayzed the cases appearing in the literature, the latter tabulating 187 cases, which apparently do not include the case which he himself reports, and in which a positive diagnosis was made. Since then I have been able to find but 2 cases reported, that of Barie and Cleret,[6] in which they made a diagnosis of Stokes-Adams disease with combined mitral and aortic stenosis and insufficiency, the tricuspid stenosis being discovered at autopsy, and that of Mackenzie,[7] in which a correct clinical diagnosis was made.

Adding to the 187 cases reported by W. W Herrick, his own case, those of Barie and Cleret, and of Mackenzie, and the 5 here reported, we have a total of 195 cases. These may be analyzed as follows:

[2] Gaz. des hôp., 1868, xli, 310.
[3] Thèse de Paris, 1888.
[4] Boston Med. and Surg. Jour., 1897, cxxxvi, 244.
[5] Archives of Internal Medicine, 1908, ii, 291.
[6] Arch. d. Mal. du Cœur, Paris, 1910, iii, 209 to 217.
[7] Diseases of the Heart, 1908, p. 304.

Sex.

Male	38
Female	141
Sex not known	16
	195

Age.

10 to 20 years	16
20 to 30 years	60
30 to 40 years	44
40 to 50 years	29
50 to 60 years	10
60 to 70 years	6
Not known	30
	195

Previous History.

Rheumatism	66
Doubtful rheumatism or chorea	11
No rheumatism	35
Not known	83
	195

Association of Valve Lesions.

Tricuspid alone	14
Tricuspid and mitral	104
Tricuspid and aortic	64
Tricuspid, mitral, and aortic	6
Tricuspid, aortic, and pulmonary	1
Tricuspid—endocardium of left auricle	1
Tricuspid, mitral, and pulmonary	12
Cases with adherent pericardium	12

Etiology. Undoubtedly tricuspid stenosis is often due to endocarditis following rheumatism, or some other acute infection. The fact that it is almost invariably accompanied by lesions of the mitral or aortic valves confirms this view. Osler states that congenital cases are not uncommon. This is supported by the opinion of other observers. These are usually accompanied by some other defect. The absence of any rheumatic history and the existence of a generalized narrowing of the whole aorta would suggest very strongly that the stenosis in Case I may have been congenital in origin. These congenitally defective valves are undoubtedy very liable to postnatal endocarditis.

Symptoms. The conspicuous symptom is the extreme cyanosis in the majority of cases. This is due to the marked venous stasis resulting from the tricuspid narrowing. Occasionally it has been absent, as in Shattuck's[8] case. Otherwise, there is nothing char-

[8] Boston Med. and Surg. Jour., cxxiv, p. 307

acteristic. Dyspnea may be extreme when broken compensation, due to over dilatation of the right auricle, supervenes. It is surprising with what degree of comfort these cases are enabled to go about for years. This is probably due to the fact that the narrowed auriculoventricular orifice lessens the engorgement of the pulmonary circulation and the consequent dyspnea. In the terminal stages of the disease, dyspnea may become extreme, even on the slightest exertion. Cough, general anasarca, and effusion into the serous sacs also supervene.

Physical Signs. I. *Inspection.* (1) A presystolic pulsation may be observed in the jugular veins and in the markedly enlarged liver if the case is seen when the right auricle is still compensating. With the striking tricuspid narrowing so often seen, the right auricle is not able to readily empty itself, and there is a consequent wave transmitted backward into the nearby venous trunks. This sign disappears in many of the cases with decompensation, as the auricular contraction is too weak to give rise to a reflux wave during auricular systole. (2) Precordial inspection reveals nothing characteristic. (3) Mackenzie considers a presystolic pulsation of the liver an important sign.

II. *Palpation.* (1) The radial pulse is nearly always extremely small in volume, owing to the overengorgement of the venous and impoverishment of the arterial systems Frequently it cannot be counted, and it is irregular in force and rhythm and of low tension. (2) A presystolic thrill may be, but rarely is, felt at the tricuspid area. It is often difficult to differentiate such a thrill from the accompanying thrill of mitral stenosis. (3) The systolic shock may be marked over the tricuspid area and was of value in arriving at a diagnosis in Case I. In this instance the exaggerated systolic tap was present at the mitral area, but was even more marked at the tricuspid.

III. *Percussion.* The distinguishing feature is increase in the area of cardiac dulness toward the right, especially in the region of the right auricle.

IV. *Auscultation.* (1) When a rumbling, presystolic murmur is audible over the lower sternal region and particularly toward the right border, it is of great value in helping to arrive at a diagnosis. Very frequently the murmur is absent owing to the weak action of the right auricle in the stage of decompensation. (2) The first sound may be snapping at the tricuspid area. This sign, together with the exaggerated systolic shock and extreme cyanosis, were the three which chiefly led us to make the diagnosis in Case I. There was no presystolic murmur at the tricuspid area. (3) The second pulmonic sound is usually said to be enfeebled. This is not always the case, however, as it may be accentuated. (4) Mackenzie has pointed out that the right auricle may become so greatly hypertrophied that it sends back a large wave into the jugular vein

with such force that it causes the valves in the jugular and subclavian veins to close with a snap, which he was able to hear over these veins as a clear, sharp sound preceding the first sound.

Regarding the diagnosis, Shattuck says: "Whether a presystolic souffle can be heard or not, tricuspid stenosis can be pretty safely diagnosticated if the patient is a female with rheumatic history, has mitral stenosis, perhaps also, aortic disease, and presents the evidences of prolonged or recurrent venous stasis of greater or less degree."

The fact that, including the cases here reported, the clinical diagnosis has been made in only 13 out of the 195 cases reported, indicates that recognition of the lesion is not easy. It is nearly always complicated by the physical signs of mitral and aortic disease and this helps to obscure the picture. Another factor must be taken into consideration, and that is, that many of the hospital cases are admitted in a moribund condition. This occurred in two instances in the present series and prevented careful study.

THE OPERABILITY OF INTRAMEDULLARY TUMORS OF THE SPINAL CORD.

A REPORT OF TWO OPERATIONS, WITH REMARKS UPON THE EXTRUSION OF INTRASPINAL TUMORS.[1]

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A study of the literature on intramedullary tumors of the spinal cord will show that almost all authors consider growths within the substance of the cord as inoperable. A few writers (Rothman, etc.) have suggested that such tumors might be operated upon, but Oppenheim, Bruns, and others only mention this possibility.

Intramedullary tumors are not by any means as rare as ordinarily they are believed to be. Thus Allen Starr,[2] quoting from Schlesinger, states that among 302 tumors of the cord, 125 were within the cord substance. These included sarcoma, tubercular tumors, gumma, glioma, lipoma, cysticercus, neuroma, cholestea-

[1] Read at the meeting of the New York Neurological Society, November 1, 1910.

[2] Text-book of Nervous Diseases, 1909, p. 442.

toma, myxoma, teratoma, adenoma (Benda), endothelioma, etc. Many of these intramedullary growths infiltrate the cord substance and increase in size by extending upward and downward, but some enlarge in their transverse diameter, are encapsulated, and of small size. Gowers[3] states that "these tumors in some cases blend with the substance of the cord, but in other instances they are bounded by an area of softening which often isolates even invading growths. Some tumors are sharply limited. The removal of such a tumor could hardly fail to cause a traumatic inflammation that would damage and perhaps destroy all of the elements of the cord at the spot and would probably be permanent in its effects."

If it can be done with little or no injury to the cord, there is no valid reason why such localized growths should not be removed. We believe that some operators have in fact removed tumors from the substance of the cord, which appeared to them extramedullary. Schlesinger[4] declares that the tumors may bulge from the cord to such a degree that on first view they give the impression that they are extramedullary.

During the past year we have twice encountered what we believe to have been an intramedullary growth of the cord,[5] and in each case, by a method to be described, have removed the tumor from its bed in the cord substance.

Case I.—*Intramedullary gliosarcoma of the cervical cord (fifth, sixth, and seventh segments); laminectomy and removal of the tumor in two stages; recovery.* Dr. B. L., aged forty-two years, was referred to the surgical department for operation from the service of Dr. J. Fraenkel on January 12, 1909, with the following history: After a sore throat in the spring of 1907, the patient began to suffer with pain in the back of the neck, of a boring character. The pain gradually spread over the shoulders and down the arms, and was followed by numbness in the right hand. For about two years these symptoms occurred in attacks, and between the attacks the patient felt well. In the summer of 1909 she first began to notice some awkwardness in the left arm, soon followed by considerable loss of power in the left arm, and later in the left leg. About this time the pains in the upper extremities grew less marked. By the fall of 1909 the awkwardness had affected also the right upper and lower extremities, and the patient's loss of power was so great that she had much difficulty in walking. Then followed a rapid loss of power in the upper extremities, especially the left, and a recurrence of the pain in the back of the neck and shoulders. Soon the lower limbs became weak and stiff.

[3] Diseases of the Nervous System, 1899, p. 609.

[4] Handbuch der Path. Anatomie des Nervensystems, 1904, p. 1109 et seq.

[5] The first patient came from the service of Dr. Fraenkel, and the second from the service of Dr. Collins. We are indebted to these gentlemen for permission to use the histories and medical records.

General condition good; well nourished. Special senses normal; no difficulty in swallowing or in urination and defecation.

Pupils are of normal size, and react well to light and accommodation.

She has to be supported when she sits up in bed; she can walk only with the greatest difficulty when supported. The cervical and dorsal vertebral column are held rigid. There is marked tenderness on percussion over the spines of the fourth, fifth, and sixth cervical vertebræ. When the attempt is made to flex the neck on the chest, the patient has a feeling of constriction around the upper part of the chest.

The motor power in both upper extremities is much diminished, but much more on the left than on the right side. When the patient attempts to move either extremity there is coarse ataxia, and she says she does not know the position of the limbs unless she looks at them. The left arm can hardly be raised away from the body; all movements at the elbow are weak; extension of the forearm is impossible. All of the muscles of the left arm and forearm react only slightly to the faradic current; no contraction of the triceps can be obtained.

There is marked atrophy of the muscles forming the thenar and hypothenar eminences on the left side, of the triceps and the infraspinatus.

On the right side there are the same changes as on the left, but very much less marked.

The motor power in the lower extremities is much diminished, especially on the left side. The knee-jerks are exaggerated, especially on the left side; double ankle clonus, Babinski, Oppenheim, left greater than right.

The sensory changes are represented in Fig. 1.

X-ray examination failed to show any changes in the vertebral column. The fluid obtained by lumbar puncture was not under great pressure, and did not contain anything abnormal.

Surgical History. January 13, 1910, laminectomy, first stage (Dr. Elsberg). Median incision over spinous processes of fourth cervical to first dorsal vertebræ; exposure and removal of spines and laminæ in usual manner; little bleeding, well controlled by packings of hot saline solution. Dura tense; no pulsation can be seen or felt. Incision in dura, 5 cm. long; escape of moderate amount of cerebrospinal fluid from above; exposed portion of cord much enlarged; no evidence of tumor on any side of cord.

In incising the dura, the smooth posterior surface of the prominent and enlarged cord was nicked in two minute spots. From the small accidental openings distinct tumor tissue began to extrude from the otherwise intact cord. The minute openings were then united by an incision in the posterior surface of the cord, and the intramedullary growth became more and more prominent. It was evidently

advisable to further enlarge the incision in the cord and allow the natural intramedullary pressure to gradually extrude the growth. The incision in the posterior column was then enlarged until it was 1 cm. long. Under the eye there then occurred extrusion of a small mass which was clearly tumor tissue, and which seemed to be connected with a larger mass within the substance of the cord.

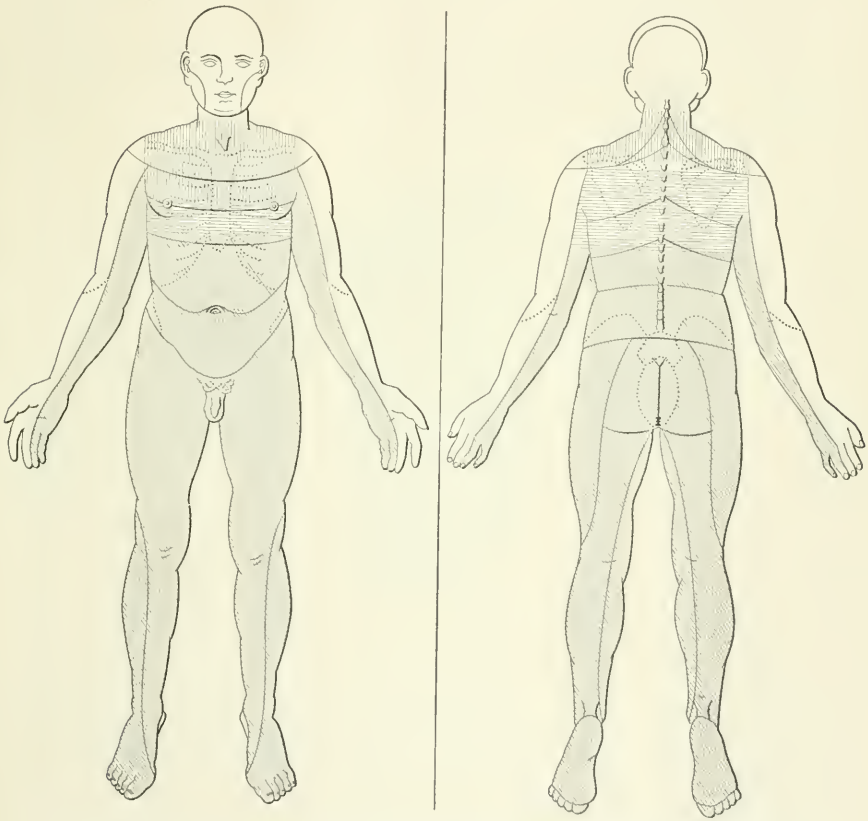

Fig. 1.—Case I. Verticals, hyperalgesia; horizontals, anesthesia; oblique lines, hypesthesia and hypalgesia.

The operation had thus far lasted only forty minutes, and little blood had been lost. The patient's condition was, however, not very good; she looked pale, and her pulse was 120, and only of fair quality. I concluded, therefore, to desist from any further manipulations for the time being. The muscles were carefully sutured, together with interrupted catgut stitches, the fascia with a continuous stitch, and the skin edges united by a subcuticular suture. Voluminous dry dressing.

The patient was in good condition on the following day, but the second operation was delayed for one week.

January 20. Ether anesthesia; dressings removed; wound had healed by primary union; wound reopened and dura and cord exposed (Dr. Elsberg).

A large tumor mass had been extruded from the cord and lay almost outside of and on top of the cord between the fourth cervical and first dorsal segments. With little difficulty, very slight handling of cord substance, and practically no bleeding, the tumor was peeled out of its bed. Three posterior nerve roots on the left side ended in a thin layer of cord tissues, which formed part of the wall of the cavity left after removal of the tumor.

Fig. 2.—Intramedullary tumor of cervical cord removed from Dr. L. in two stages.

After careful cleansing of the cavity the edges of the pia were sutured together with fine catgut; the dura closed by a running suture of fine silk, and the muscles and skin united by catgut sutures. Dry dressing. Duration of operation, fifty-five minutes; condition of patient at end of operation good; pulse 108, and of good quality; respirations regular and deep.

The tumor that had been removed was of a reddish-brown color; soft and edematous; it measured 5.3 by 2 cm., weighed 15 grams. The specimen (Fig. 2) was examined by Dr. F. S. Mandlebaum, director of the laboratory of the Mt. Sinai Hospital, who reported it to be a gliosarcoma.

The patient made a rapid recovery from the operation. The wound healed by primary union, and all dressings were discarded after the second week.

For the first few days after the operation the weakness in the extremities and the sensory disturbances were somewhat more marked. Rapid improvement followed. By the end of the fourth week the

patient was able to sit up out of bed, without assistance. The muscular power in the limbs improved rapidly; by the time she sat up out of bed, she had regained practically all of her power in the right and very much power in the left upper limb. The paralysis of the triceps had disappeared. The muscular power in the lower extremities returned somewhat more slowly, but there was a constant and steady improvement.

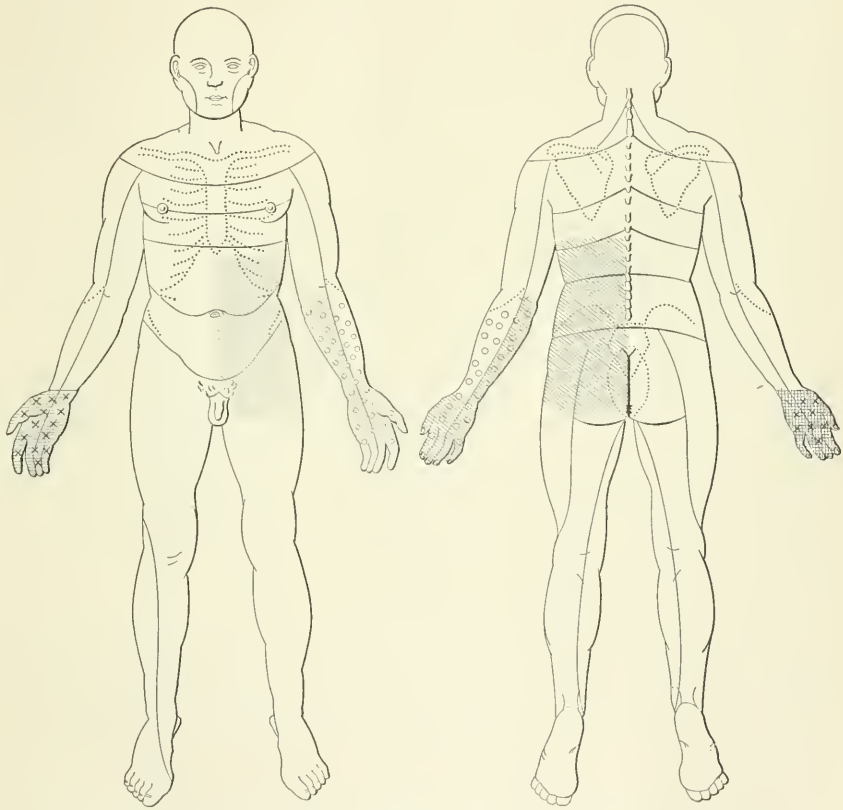

FIG. 3.—Case I. Sensory disturbances eight weeks after the removal of the tumor; areas shaded similar to those in Fig. 1. Crosses, hyperalgesia to hot and cold; circles, analgesia to heat and cold.

By the beginning of March (two months after the operation) she was able to stand on her feet and take a few steps when well supported; but her lower limbs, especially the left, were still very ataxic. Most of her sensory disturbances had by this time disappeared (Fig. 3).

At the present time, eight months after the operation, she can write and use the typewriter, and can walk considerable distances

without support. She still has some hyperesthesia in the left hand, and her lower limbs, especially the left, are still somewhat stiff. She is steadily improving. This improvement has been much aided by thorough massage and exercises, which have been given her by Dr. Wolf of this city.

Remarks. This case is of unusual interest. The patient was transferred to the surgical department by Dr. Fraenkel, with the diagnosis of tumor of the cord between the fourth and seventh cervical segments.

At the second operation we were not absolutely certain that the tumor was a true intramedullary one, and considered that possibly, in spite of the fact that underneath the pia part of the lining wall of the tumor was formed by tissue containing the superficial origin of several nerve roots, and that we had incised the cord substance in order to allow the tumor to extrude, the tumor had simply been one underneath the pia which had grown into the cord in such a way that the cord bulged around the tumor. A more careful study combined with the experience that we had in a similar case which came to autopsy, and in which a careful examination of the cavity of the cord was made for us, has convinced us that both were cases of intramedullary growths of the cord. At the first operation the small accidental incisions into the cord and the subsequent more liberal incision on the posterior aspect of the cord proper exposed the intramedullary tumor. At the second operation the large extruded growth had been squeezed out of its intramedullary bed, and could be lifted up and peeled off with ease, leaving the wall of the cavity in the cord. On the left side, three posterior nerve roots could be seen running into the thin shell of the cord, which at this point had enveloped the neoplasm.

Case II.—*Intramedullary tumor (glioma) of the cervical cord (fourth to sixth segments); laminectomy and removal; death in four hours from respiratory paralysis.* Sarah B., aged forty years, was referred to the surgical department with the diagnosis of tumor of the cervical cord, from the service of Dr. Joseph Collins, on February 18, 1910.

About two years before, the patient began to have pain in both upper extremities, and at the same time noticed that her arms were becoming weak. The left arm was affected more than the right, but the symptoms began at the same time in both limbs. The limbs gradually became weaker, and about one year later she began to have attacks of pain in her abdomen.

For the last six months the patient has been unable to walk or to use her lower limbs, and for two months she has not had control of her urine.

The patient was in poor condition when admitted into the service of Dr. Collins, so that it was impossible to obtain much history from her. She frequently contradicted herself.

She was much emaciated; her pulse was very weak; she was constantly wet from incontinence of urine.

Marked tenderness to percussion over the third, fourth, and fifth cervical spines. Decided atrophy of interossei on both sides of upper extremities; marked flattening of thenar and hypothenar eminences. Arms do not seem atrophied. Flexion of forearms on arms is good; extension is decidedly weak; there is only a weak contraction of the triceps muscle; all movements of arms and forearms are weak; reflexes at elbows and wrist-jerks cannot be obtained.

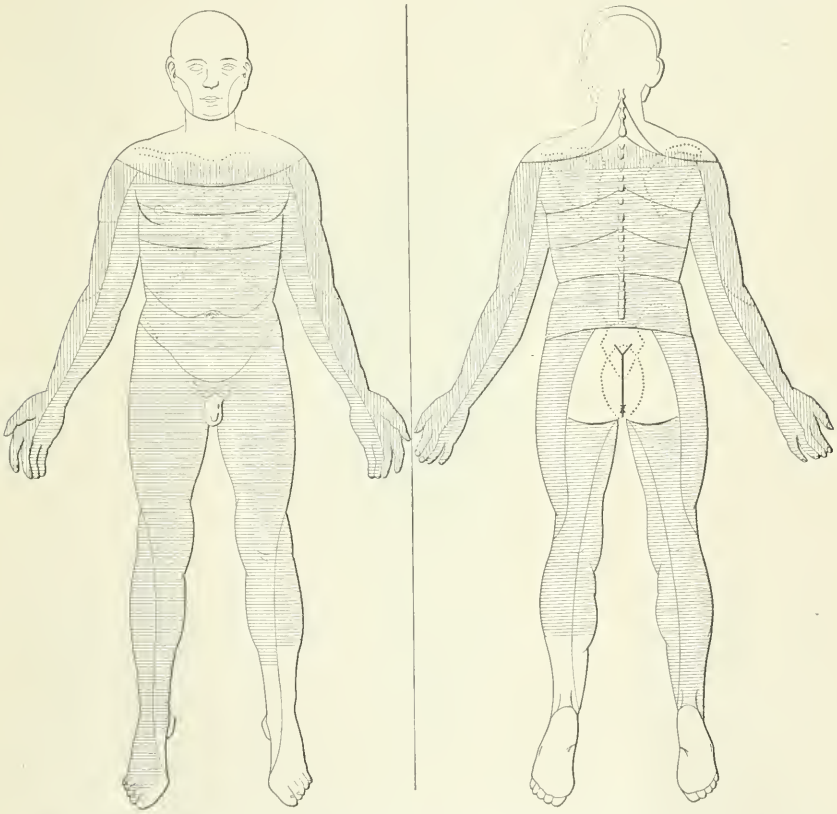

Fig. 4.—Case II. Sensory disturbances before the operation. Shading similar to that in Fig. 1.

There is complete paraplegia, with increased knee-jerks, ankle clonus, Babinski, Oppenheim, and Mendel-Bechterew.

For sensory changes see Fig. 4.

There is marked tenderness to pressure over the spinous processes of the third, fourth, and fifth cervical vertebræ, especially over the fourth.

February 19. Patient has been rapidly growing weaker. She

is frequently cyanosed, and has difficulty in breathing. At times her pulse is almost imperceptible.

February 19. Laminectomy (Dr. Elsberg). Removal of fourth, fifth, sixth, and seventh cervical and first dorsal spines and laminæ in the usual manner. In the upper part of the exposed dura the pulsation was marked; below no pulsation could be observed. Incision of the dura for 5 cm.; cord appears much distended between fourth and sixth segments; palpation of cord substance reveals in this region a marked tumefaction of this part of the cord. Above the affected area the cord looks soft and pulsates markedly, while the part of the cord in which the tumor lies does not pulsate. A small incision was now made in the pia over the most prominent part of the cord in the median line; at once a part of a tumor mass bulged through the cord tissue. The incision was then lengthened

Fig. 5.—Intramedullary tumor of cervical cord removed from the patient, Mrs. B.

and deepened, when the tumor at once began to bulge out of the cord substance. The intramedullary pressure seemed so great that in a few minutes the larger part of the growth was extruded. As it was well encapsulated, it was lifted out of its bed with ease, and with practically no bleeding. After the wound in the cord had been thoroughly irrigated with saline solution, the cavity in the cord with the overlying pia was closed by interrupted sutures of fine silk, and the dura and soft tissues closed in the usual manner.

The tumor (Fig. 5) measured 4½ by 2 cm.; it was of a yellow color, and fairly hard. The microscopic examination revealed it to be a cystic glioma.

The entire operation had lasted less than forty minutes. At the conclusion, the patient looked slightly cyanosed, although the respirations were regular and deep. The pulse was weak, and varied between 112 and 120. The character of the pulse was no worse than it had been at the beginning, and the patient did not look at all shocked. Three-quarters of an hour later she was fully awake, and asked for water; she was still slightly cyanosed, and her breath-

ing had a jerky character. Two and one-half hours later she suddenly became pale, her pupils widely dilated, and no pulse could be felt at the wrist. A few minutes later the breathing stopped. In spite of active stimulation, artificial respiration, intratracheal insufflation of oxygen, her heart action became rapidly poorer until death occurred.

At the postmortem examination the wound was found in perfect condition; there were no clots in the cavity in the cord (Fig. 6).[6]

Remarks. This patient grew worse so rapidly that operative interference, if done at all, had to be done without delay. The removal of the tumor, after its exposure, occupied two or three

Fig. 6.—Part of cervical cord of Mrs. B.: *A*, dura; *B*, pia; *C*, cord tissue with origins of posterior nerve roots; *D*, cavity in substance of cord left after removal of tumor, *E*, cord.

[6] We are indebted to Dr I. Strauss, of the Cornell University Medical School, for the examination and following report on the tumor and cord:

"The tumor is a very cellular glioma. The piece of growth examined has a thin capsule, which contains bloodvessels and stains red with Van Gieson stain.

"The section of the spinal cord shows an absence of the posterior columns, which is due to the presence of the growth in this region. The posterior horns of the gray matter are present, and the posterior roots and their entrance zones are preserved. The bases of both posterior horns are abnormally vascular, probably because of the attachment of the tumor. The anterior wall of the central canal can be recognized from the presence of a few epithelial cells, which lie dorsally to what remains of the anterior commissure. The posterior wall has been destroyed by the growth or through its removal. The anterior horns and their ganglion cells are fairly well preserved. The anterior spinal vessels, both artery and vein, are unusually large and tortuous, and suggest that they may have been concerned in furnishing the blood supply to the tumor."

minutes, and we therefore felt that it was justifiable to do the entire operation in one stage. The dura was fully exposed within ten minutes after the incision of the skin, and the tumor was out within twenty-two minutes of the first incision.

It is very possible, however, that the unfortunate outcome might have been prevented if the operation had been done in two stages. The extrusion of the tumor occurred under the eye, and it would have been better to have allowed the cord structures to have accommodated themselves to their new relations before the actual removal of the tumor.

The above two operations for intramedullary tumors of the cord demonstrate that localized growths of the cord substance must not be considered as inoperable. They should be attacked by the neurological surgeon as readily as subcortical tumors of the brain. The results should be at least as good as those obtained in subcortical intracranial growths. A small incision in the lumbar cord near the posterior median fissure will injure only sensory fibers from the posterior roots of some sacral nerve fibers which regularly degenerate upward when the lower lumbar and sacral posterior nerve roots are divided. These sacral fibers at first occupy a position near the posterior median fissure of the cord, and in their upward course gradually come to lie nearer and nearer to the posterior surface of the posterior median column. The lumbar, dorsal, and cervical ascending fibers lie in order farther and farther forward, and are not apt to be injured when a superficial incision in the posterior column near the median line is made. The main bundles of descending fibers in the posterior columns lie in situations where they are not apt to be injured.

From the above description of the course of fibers as given by Van Gehuchten, it follows that a small incision in the posterior median column will injure or divide fine ascending fibers which are derived from the posterior root fibers of the sacral, lumbar, and perhaps lower thoracic nerves. After having travelled a short distance in the posterolateral white column (column of Burdach), they run up the posteromedian column (column of Goll) into the medulla oblongata.

Based on the anatomical grounds above stated, the writers suggest the following method of treatment for intramedullary tumors of the cord. If after laminectomy and incision of the dura the surgeon finds that he has to deal with a localized intramedullary growth, he should make a small incision, about 1 cm. long, in the posterior median column a few millimeters outside of the posterior median fissure, at the spot where the growth seems to be nearest the surface of the cord. The incision should be deep enough to cut the pia and the substance of the column down to the tumor. The tumor will then begin to bulge through the incision. No matter how markedly the tumor will seem to bulge, the surgeon must not

attempt to remove the growth, for he will be sure to cause grave injury to the cord. He must leave it to nature to extrude the tumor. As the normal intramedullary pressure will tend to readjust itself, the growth, which has caused an increased pressure, will be gradually pushed out of its bed. Nature will do this by a slow and gradual process, and the tumor will be slowly extruded, with a minimum of injury of nerve fibers. Therefore, after the small incision into the cord has been made, the muscles and skin must be closed and the actual removal of the growth left to a second operation.[7] After about one week the wound is reopened and the tumor, which will in all probability be found outside of the cord, can be removed by dividing the few adhesions which remain. If the manipulations are done with delicacy and care, no injury should be done to the cord substance. When the tumor has been removed, the pia should be closed by fine silk sutures, and the dura, muscles, and skin sutured in the usual manner.

In the case of intramedullary tumors which extend over a large number of segments, and which infiltrate the cord substance, a small incision into the cord made in the manner above described at the level of the most marked symptoms, may allow of the partial extrusion of the tumor, with perhaps amelioration of the symptoms.

It is not at all beyond the range of possibility that some cases of spinal gliosis, syringomyelia, and hematomyelia will come into the domain of the surgeon. It is perfectly feasible to drain a central cavity in the cord into the subdural space, and perhaps prevent the symptoms due to pressure of the fluid upon the nerve fibers. In the same way it may be possible to benefit certain cases of hematomyelia by allowing the blood clot to be extruded from the substance of the cord.[8]

The method of treatment above described we have called the "extrusion of intramedullary tumors." We believe that the application of the principle of extrusion to the surgery of intramedullary growths of the cord will open up a new field to neurological surgery. The cases which are reported in this paper are presented as evidence in favor of this view.[9]

[7] In a recent paper (The Special Field of Neurological Surgery, Five Years Later, Bulletin of the Johns Hopkins Hospital, November, 1910) Cushing gives a short description of a case of glioma in the substance of the cord, in which he made an incision in the posterior column and removed a specimen for examination. The improvement in the patient's symptoms was so marked that, Cushing states, "she has so far recovered as to make us regret that the posterior column was not slit throughout the whole length of the exposed and tense cord." Perhaps the improvement was due to the gradual extrusion of the tumor.

[8] In the case of a recent patient from the service of Dr. Bailey, who was operated upon by Dr. Beer, an extensive intramedullary clot was found in the dorsal cord. The intramedullary clot was treated by the method of extrusion. Much old blood was extruded from the cavity in the cord. The condition was probably one of hemorrhage into a cystic glioma or into a cavity of syringomyelia. The patient has fully recovered from the operation, and there has been considerable improvement, but it is too early to say how great the improvement will be.

[9] In a paper published in October, 1909, Zenner and Kramer made a similar suggestion regarding the possibility of the delivery of brain tumors "by the pressure from behind."

ACUTE PHLEGMONOUS GASTRITIS DUE TO THE STREPTOCOCCUS PYOGENES.

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Acute phlegmonous gastritis is a comparatively uncommon finding on the postmortem table. Schnarrwyler,[1] in 1906, reviewed 83 cases that had been reported up to that time. Robertson,[2] in 1907, reported 2 cases of his own and reviewed the previously reported cases, which numbered 89. More recently Adams[3] has reported a case due to the pneumococcus. The literature upon this subject will be found in the papers referred to above.

The chief cause of acute phlegmonous gastritis is the streptococcus, but there are several cases in which the pneumococcus was found, and a few in which the condition was due to other bacteria.

The case here reported points to the symptom of sudden and severe epigastric pain as the salient clinical feature of the disease, and is of interest from both the pathological and bacteriological points of view.

E. B., male, aged thirty years, was admitted in the service of Dr. Lafleur at the Montreal General Hospital, April 26, 1910, complaining of shortness of breath and swelling of the legs.

Personal History. The patient was born in England, had scarlet fever and measles in childhood, gonorrhea at fifteen and a severe attack of typhoid fever in 1905. He was in the habit of taking one or two glasses of beer or whiskey each day, and smoked to excess, six to seven pounds of tobacco a month.

Family History. His father died aged forty-seven years, from cardiac disease, his mother of Bright's disease, aged twenty-eight years. One sister died of puerperal septicemia; three brothers and one sister are living and well.

Present Illness. February 25, 1910, after a hard day's work, he began to have dyspnea and severe pain in the right side and epigastric region. He was subsequently unable to work on account of the dyspnea. His appetite was poor and there were frequent attacks of vomiting. The pain in the right side and epigastrium were constant. On April 23 swelling of the legs was noted and the dyspnea became urgent (orthopnea). On admission the pulse was 136, irregular, of small volume and low tension; the respirations were rapid. The heart was enlarged, the sounds irregular, and there

[1] Archiv f. Verdauungskrank., 1906, xii, 116.
[2] Jour. Amer. Med. Assoc., December 28, 1907, xlix, 2143
[3] Lancet, January 29, 1910, clxxviii, 292.

was an apical systolic murmur transmitted to the left axilla. There was edema of the legs and thighs, tenderness over the epigastrium, and slight muscular resistance over the upper part of the abdomen. The tongue was coated. As soon as food was taken vomiting occurred. The liver was palpable.

He was discharged May 14, 1910, improved.

On June 9, 1910, the patient was readmitted. Soon after he left the hospital the general signs and symptoms which were present on his first admission recurred. The physical examination at this time showed an increase in the cardiac dulness and marked irregularity of the heart rhythm. There was evidence of fluid in the right pleural cavity. The tongue was coated and the breath foul. The abdomen was prominent, but there was no abdominal tenderness or rigidity. There was no dulness in the flanks. The liver was still palpable. The spleen was not enlarged.

The patient did not improve, although the edema disappeared. There was dyspnea, pain in the epigastrium, and over the precordium. Severe hiccough, with vomiting, developed and persisted.

On June 16, 1910, an area of erysipelas appeared on his nose and soon spread over both cheeks. The temperature was elevated and the precordial pain and dyspnea became more marked. The patient soon became delirious, restless, and very noisy. The tenderness over the epigastrium remained acute. On June 19, 1910, he became much worse, and complained of a sudden acute pain in the epigastrium. The pulse failed, and after severe dyspnea he died.

Autopsy. No. 107, 1910. June 19, 1910. Dr. Baird. E. B., aged thirty years; body length, 170 cm.; hour, 9.30 P.M. Service of Dr. Lafleur.

The body is that of a well-developed and well-nourished white male adult. Rigor mortis is general and well marked. There is lividity of the dependent parts and cyanosis of the face, ears, neck, and tissues beneath the finger nails. The pupils are unequal, the right 9 mm.; left, 6 mm. Slight edema over the shins and ankles. There is a dusky red, fairly sharply outlined area over the bridge of the nose and cheeks, throughout which the tissues are thickened, puckered, and of a leathery consistency.

Peritoneal Cavity. The subcutaneous fat is normal. The abdominal muscles are firm, dark red, and well developed. The peritoneum is covered with a viscid exudate, and its bloodvessels are deeply injected. In the pelvis and recesses of the peritoneum there are over 300 c.c. of thick, yellowish fluid, smears from which show Gram positive cocci in short and long chains. There is a yellowish exudate on the under surface of the diaphragm and upper surfaces of the liver and spleen. The stomach is greatly distended, dark bluish red in color; its lower border extending almost to the level of the umbilicus. The intestines are free from obstruction. There are a few small areas of necrosis in the fat about the cardiac

end of the stomach. The subperitoneal and retroperitoneal tissues in the region of the left adrenal gland are edematous. The tissues about the left crus of the diaphragm are thickened and moist. On incision purulent material escapes. The mesenteric lymph nodes are enlarged, pale, and soft. The diaphragm reaches to the fifth rib on the right side and the fifth interspace on the left.

Pleural Cavities. There are no adhesions. The bloodvessels of the right pleura are deeply injected and the pleural cavity on this side contains 350 c.c. of turbid yellow fluid, smears from which shwo Gram positive cocci in short and long chains. The bloodvessels of the left pleura are less injected than those of the right and the cavity itself contains very little turbid fluid. Smears from this fluid also show Gram positive cocci in short and long chains.

The pericardial cavity is enlarged, its wall is of normal thickness. The serosa is smooth, moist, and glistening. There are 120 c.c. of clear yellow fluid present, smears from which show no organisms.

Heart. Weight, 500 grams. It measures 17 by 12.5 cm. in its longest diameters. The epicardium is generally smooth, and its bloodvessels moderately injected. Shining through the epicardium of the left ventricle are two round, elevated, light yellow, edematous areas each about 1 cm. in diameter. Smears from these show Gram positive cocci in short and long chains. The chambers of the heart are widely dilated, particularly the right ventricle, and contain blood-stained serum and postmortem clot. The myocardium is of normal consistence; that of the left ventricle is slightly thickened. The endocardium is normal. The valves are normal, except the posterior aortic cusps, which are sclerosed, much thickened, and show fenestration of their edges. The coronaries are normal. T. V., 15; P. V., 9.5; M. V., 10; A. V., 9; L. V., 2; R. V., 0.7.

Lungs. These organs are voluminous and dark red. On the posterior surface of the right lower lobe there is a round, elevated, firm, very dark red area 2 cm. in diameter. Section of the lobes shows marked congestion, and dark, frothy, blood-stained serum exudes on slight pressure. The dark red area noted above is of a much deeper red, firmer than, and is sharply separated from, the surrounding lung tissue. This area extends from the pleural surface into the lung tissue in an irregular wedge-shape.

Spleen. Weight, 310 grams, dark red. The capsule is covered with a viscid, yellowish exudate. On section the surfaces are dark red, soft, and moist, and pulp comes away freely on scraping. The Malpighian bodies are just visible.

Gastro-intestinal Tract; Stomach. This organ is markedly dilated. The bloodvessels beneath the peritoneal surface are injected. The stomach contains thin, yellowish, turbid liquid. The mucosa is generally a deep red, has a velvety appearance, and is covered with a thin tenacious layer of yellowish mucoid material. Tension shows that the deep red color is not uniform but occurs in small

areas 2 to 4 mm. in diameter, separated by narrow pale bands. There are no ulcers. The wall of the stomach for a distance of 15 to 18 cm. from the esophageal orifice varies in thickness from 4 to 8 mm. On section this thickening is seen to be due to puriform infiltration of the submucosa which exudes drops of thin, yellowish pus, smears from which show leukocytes and chains of Gram positive cocci. The esophagus appears normal. The mucosa and coats of the duodenum, jejunum, and ileum are normal. The intestines contain fecal material; the mucosa in general has a pink cast.

Pancreas. Appears normal.

Liver. Weight, 1930 grams. The surface has a mottled, yellowish-red color, and near the left border of the posterior surface of the left lobe there is a deeply injected area. The edges are sharp. On section the surfaces have a greasy appearance and are of a mottled, yellowish-red color. The mottling is due to light yellow areas, varying from 1 to 4 mm. in diameter, which are separated by deep red intercommunicating bands. The liver tissue is softer than normal.

The gall-bladder is much distended and its walls are thin. Apparently there is no obstruction to the bile passages, for on exposure of the papilla of Vater bile can readily be forced out in a large stream and a probe easily passes into the common and hepatic ducts. On opening the gall-bladder two moderate sized faceted calculi are found.

Kidneys. Weight, 450 grams; enlarged, dark red, and smooth. The capsules strip readily, leaving smooth surfaces. The cortices are pale and of normal width. There is no edema. The pyramids are well defined; the pelves and ureters normal.

Adrenals. The right appears normal; the left is slightly enlarged and very deeply injected.

Bladder and Genital Organs. Normal.

Aorta. There is no sclerosis. The intima is of a deep red color throughout, appearing as if stained with red ink.

Organs of the Neck. Normal.

Brain. Weight, 1425 grams, and is normal.

Middle Ears, Nasal Sinuses, and Bone Marrow. Normal.

Anatomical Diagnosis. Acute phlegmonous gastritis; acute pleuritis; empyema; acute pericarditis; acute general peritonitis; erysipelas; central necrosis of the liver; septic spleen; cellulitis of the left crus of the diaphragm; necroses in the fat tissue about the cardia of the stomach; congestion and infarct of the lungs; cardiac dilatation and hypertrophy.

Sharlach R. Heart, spleen, kidney, no fat. Liver, cells about central veins contain fine droplets of fat.

Bacteriological Report. Cultures were made from the heart's blood and the walls of the stomach. From both of these sources a pure culture of Streptococcus pyogenes was obtained.

Microscopic Examination. Heart. The myocardium appears normal except that between the muscle fibers, near the epicardial surface, there are a few groups of cocci. There is no inflammatory reaction about them. The capillaries of the epicardium are deeply injected. The endocardium is normal.

Lung. Section 1: Very marked injection throughout. The alveoli are generally normal. Situated immediately beneath the pleura there is a sharply outlined area throughout which the blood-vessels and alveoli are widely distended with blood and contain a small amount of fibrin. The walls of the alveoli within this area are not distinguishable as such and are represented by faint eosin-staining bands except those just beneath the pleura, where they are better preserved. Section 2: The alveoli contain desquamated epithelium and large cells phagocytic to pigment.

Spleen. The Malpighian bodies are normal. The pulp contains a great deal of blood, in some places obscuring the lymphoid elements. There are several groups of cocci in the sinuses. The capsule is infiltrated with lymphoid and plasma cells. The arteries show some hyaline change.

Liver. The bloodvessels in the portal tissue are distended with blood. The liver cells occur as single isolated cells and short columns and groups of cells. The latter are in the peripheral portions of the lobules, are sharply separated from an inner hemorrhagic zone, and they stain deeply with eosin. There are but few liver cells recognizable in the midzonal and central portions of the lobules. They are irregularly distributed, stain poorly, generally contain vacuoles, and show varying stages of degeneration. The anatomical situation of the columns of liver cells in the inner two-thirds of the lobule is represented by poorly defined intercommunicating bands of eosin-stained material composed of a small amount of fibrin, finely granular eosin-staining material, an occasional poorly staining liver cell, a few polymorphonuclear leukocytes, numerous red blood corpuscles, cocci and endothelial leukocytes filled with yellowish pigment. The sinusoids at the periphery of the lobules are easily distinguished and contain coagulated serum and blood cells, but throughout the inner two-thirds of the lobule the sinusoids, as a rule, cannot be made out. There is no increase of connective tissue. The capsule contains a few lymphoid and plasma cells and polymorphonuclear leukocytes.

Pancreas. Normal.

Kidney. Marked injection of the bloodvessels. The epithelium of the convoluted tubules is swollen, granular, projects irregularly into the lumina, and stains poorly. The epithelium of the collecting tubules is for the most part desquamated. The glomeruli are injected, and show some hyaline change in the walls of their capillaries. Capsule normal.

Adrenal. Marked injection of its bloodvessels. There are a few lymphoid and plasma cells, and groups of cocci in the medulla.

Stomach. The following description is based upon a number of sections taken from the cardiac half of the stomach and stained by several methods.

The bloovessels are everywhere distended with blood. The mucosa, submucosa, and muscular coats show an infiltration with cells of acute inflammation. The mucosa for the most part shows only a slight degree of cellular infiltration. The lumen of some of the glands are distended with polymorphonuclear leukocytes, and in some places there are small areas of necrosis, situated both in the superficial and deep layers of the musoca.

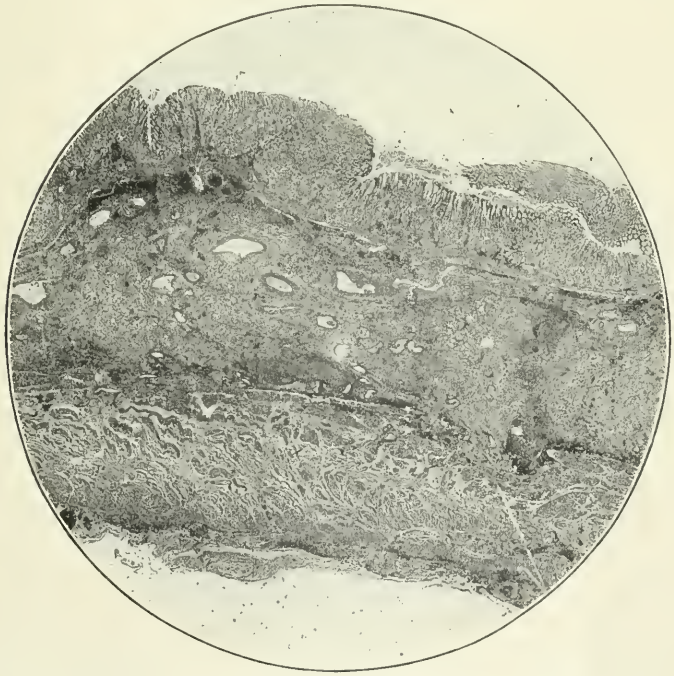

FIG. 1.—Section of stomach (low power). Note the thickened, infiltrated submucosa. The dark area to the right is shown in Fig. 2.

Between the tissues of the muscularis mucosa there are a few cells similar to those seen in the submucosa. The submucosa shows extensive necrosis, and is greatly thickened by polymorphonuclear leukocytes, small lymphocytes, red blood corpuscles, and coagulated serum. Polymorphonuclear leukocytes predominate and occur diffusely distributed through the tissue, and in small compact areas that are due to lymphatics which are distended by these cells. A similar exudate is seen in the muscular coat, but the tissues

of which it is composed are not separated as much as those of the submucosa.

There are numerous groups of cocci in the stomach wall.

A section through the esophagus at the cardiac opening of the stomach shows the submucous and muscular coats infiltrated with exudate similar to that in the stomach.

Intestine. Normal.

Lymph Node. (From the gastrohepatic omentum.) The sinuses are distended with blood. There are numerous polymorphonuclear leukocytes in the pulp and sinuses, and in the sinuses there are also many endothelial leukocytes, phagocytic to cells.

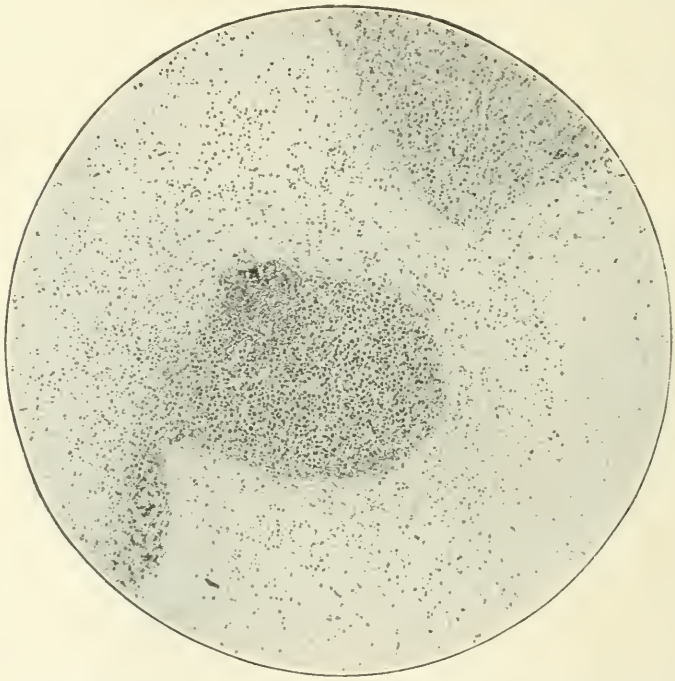

FIG. 2.—Submucosa (high power), showing lymphatics distended with polymorphonuclear leukocytes.

Phlegmonous gastritis may follow lesions in the stomach itself, or it may be secondary to an acute infection elsewhere in the body, or part of a general septicemia. It is often difficult or even impossible to determine the primary lesion. This is especially true when the stomach is but one of several organs involved and the duration of the lesions in these organs is apparently the same. Even where no ulcer is demonstrable, the stomach may be considered as the primary source of infection if this organ alone is involved,

or if the acute lesions associated with it can be demonstrated to be secondary to it.

In the case reported here where there was erysipelas, acute pleuritis, acute pericarditis, acute peritonitis, and general septicemia, it is most probable that the erysipelas was primary, and the other lesions were a part of a general bacteriemia. The following may be suggested in favor of such a view: (1) Streptococcus is the common cause of erysipelas. (2) The phlegmonous gastritis in this case developed three days after erysipelas of the face. (3) There was a general bacteriemia due to the streptococcus. (4) This organism was recovered in pure culture from the stomach wall. (5) The acute lesions elsewhere in the body were apparently of the same duration as the one in the stomach, and from them the streptococcus was recovered.

In conclusion I wish to thank Dr. S. Burt. Wolbach and Dr. Lawrence J. Rhea for assistance in the preparation of this paper.

CARDIAC MURMURS DURING ATTACKS OF BILIARY COLIC.[1]

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A few years ago I called attention in a short paper[2] to the development of heart murmurs during attacks of biliary colic. Some time later, Dr. Babcock,[3] of Chicago, published an exhaustive article on the relation of the heart to diseases of the biliary tract, and within the past few months Dr. William J. Mayo,[4] in a brief but masterly discussion of diseases of the gall-bladder, made reference to concomitant heart affections. Aside from these, the literature is meager, and yet the subject has considerable practical importance. It is not my purpose to envisage the relation of the heart to the biliary tract in its entirety, but to recur briefly to the perplexing murmurs, of which, since my first paper, I have seen several additional examples. Among 56 cases of gallstone disease from private and consulting practice, 6, or 10.7 per cent., showed cardiac murmurs. This percentage does not express the real frequency of the murmur, as not all of the 56 cases were seen during or

[1] Read at the Fourteenth Annual Meeting of the American Gastro-enterological Association, Philadelphia, April 19, 1911.

[2] The Development of Cardiac Murmurs during Attacks of Biliary Colic, Jour. Amer Med. Assoc., May 11, 1907.

[3] Chronic Cholecystitis as a Cause of Myocardial Incompetence, Trans. Assoc. Amer Physicians, xxiv, 43.

[4] Jour. Amer. Med. Assoc , April 8, 1911.

soon after an attack of colic. I believe that if the heart is carefully examined at such times the murmur will be found in a much larger proportion of cases. Of the 6, 4 were operated upon; 1 passed five stones in the feces, and 1 has had several typical attacks, but has so far not had an operation. In 5, either the physician in attendance or I myself had examined the patient prior to the attacks and had determined that a murmur was not present. In the sixth case, a woman who had suffered from gallstone colic for seventeen years, the murmur had existed for some time before I first saw the patient.

The murmur is usually quite loud and blowing, systolic in time, and is heard best at the apex. It is not transmitted far, but at times may be heard near the anterior border of the axilla. The heart is nearly always somewhat enlarged, but the dilatation is not extreme. Soon after the attack, or after an operation if one is undertaken, the murmur disappears. In one of the cases, cited in my first paper, the patient, who had had a loud blowing murmur at the height of the attack, when seen again fifty-one days later, had normal heart sounds. An operation had been performed soon after I had seen him and a large solitary stone had been removed from the common bile duct.

Regarding the significance of the murmur, the point of chief practical importance is the bearing the discovery of the murmur may have on the attitude of the physician or surgeon toward a contemplated operation. This attitude will depend to some extent on the explanation given for the cause of the murmur. Several explanations are possible. The murmur might be due to an old-established valvular heart disease antedating the formation of the gallstones. Personally, I cannot recall such a case. I have seen active pulmonary tuberculosis and gallstone colic together—and a more pathetic picture than that presented by the unfortunate woman so afflicted can scarcely be imagined—but never have I observed a genuine attack of biliary colic in a patient with typical endocarditis that had preceded the gallstone disease. (I do not, of course, mean to infer that such a condition is impossible.) In the sixth case cited above, in which the murmur had probably been present for some time, the gallstone disease had existed many years before the murmur appeared.

The murmur, I take it, is a sequel or an effect of the gallstone disease. It is probably not due to an acute endocarditis, since it disappears, as I have said, soon after the attack of colic or after an operation. It cannot be attributed to the jaundice, for it is found in cases without, as well as in cases with jaundice. I am of the opinion that the murmur depends on a myocardial weakness with temporary relative insufficiency of the mitral valve. At first I was inclined to attribute it chiefly to the pain, but wider experience has led me to the conclusion that the chronic infection of the biliary passages present in many cases of gallstone disease leads to a

degeneration of the myocardium.[5] During the attack of pain there is a sudden rise in blood pressure, and this is the exciting cause of the dilatation and of the mitral murmur.

I was confirmed in the views here expressed by the following case: Mrs. R. M., aged sixty-one years, had had one or two attacks of biliary colic prior to the one in which I first saw her. I found a mitral murmur and a slight degree of jaundice. The murmur disappeared within a few weeks. After a period of several months' comfort, another attack of colic occurred, and the murmur returned. Though the pain and the acute tenderness in the gall-bladder region accompanying this attack quickly subsided, the patient was left with a peculiar condition characterized by sudden alarming attacks of cardiac dilatation. These would come on without warning and be accompanied by intense dyspnea—orthopnea, marked cyanosis of the lips and face, usually a fear of impending death, and great prostration. The murmur, though less loud, persisted. No medicine or regimen seemed to have any influence on the condition, and gradually the patient became more and more despondent and feeble. Fearing that the attacks would ultimately prove fatal and that surgical intervention involved the lesser risk, the patient was advised to have an operation. Because of the cardiac attacks rather than because of the presence of the murmur itself, we were anxious as to the outcome, but the patient had a good convalescence, despite an ether pneumonia of limited extent. A single stone was found in the common duct. Since the operation about ten months have elapsed and the patient has had no return of her former attacks and the murmur has long since ceased to be audible.

There can be no doubt that the gallstone disease and the alarming attacks of cardiac dilatation stood in relation of cause and effect. When the one was removed, the other disappeared—*sublata causa, tollitur effectus*. The murmur, which disappeared with the improvement in the condition of the heart, must have been the result of the myocardial degeneration induced by the gallstone disease.

The case further indicates that even in the presence of serious weakness of the heart muscle, an operation may be well borne. With regard to the murmur, experience leads to the conclusion that it should not be looked upon as a contraindication to operation. Rather should it be viewed as an indication for surgical intervention, as it implies the existence of a myocardial degeneration that will grow worse if the gallstone disease is allowed to continue. Care should of course be taken to make the operation as brief as possible, and to have a competent anesthetist. The immediate after results of the operation do not seem to be complicated by the cardiac condition.

[1] A condition somewhat analogous is found in certain cases of fibroid tumor of the uterus.

It has occurred to me that the murmur might also have a diagnostic value. Given a case of repeated attacks of severe epigastric pain of obscure nature, in which angina pectoris and the crises of locomotor ataxia have been ruled out, the development of a murmur should put us upon our guard as to the possibility of gallstone disease.

I may add in conclusion that I have recently examined a number of cases of renal colic at the height of the attack without finding any cardiac murmur.

HUMAN TRYPANOSOMIASIS.[1]

REPORT OF A CASE, WITH SPECIAL REFERENCE TO THE TREATMENT.

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The case of trypanosomiasis, here reported, contracted the disease in June, 1907, on the Congo, above Stanley Pool. Fever appeared on July 12, 1907, and the parasites were found by Dr. Broden, at Leopoldville, on the 19th, and treatment was immediately begun. The patient remained in Africa until the autumn, when he returned to England. At Liverpool, Dr. Breinl (Liverpool School of Tropical Medicine) repeatedly found parasites. In October, 1907, he went to London, where he was under the care of Sir Patrick Manson,[2] who has reported the findings up to December, 1907, at which date the case was referred to me by Sir Patrick Manson.

The following record covers a period of four years of almost continuous observation. The patient had repeated paroxysms of fever from December, 1907, to November 10, 1910, about three years. During this time, part of which he lived in my house, he was under constant observation. Since the subsidence of fever he has been under examination from time to time, and continues so up to the present, October, 1911.

It is the object to report here more especially the treatment employed, introducing the clinical features of unusual importance only, or such as have relation to the treatment.

Ten years only have elapsed since the trypanosome was detected in man by Forde, at Gambia (1901), and confirmed and named by Dutton, Trypanosoma gambiense. It is less than this (about

[1] Read before the Association of American Physicians, May 10, 1911.

[2] Ann. Trop. Med. and Parasit., March, 1908, ii, No. 1, 46.

eight years) since trypanosomatic fever was recognized (by Castellani Bruce, Nabarro, Greig, and others) as the first or earlier stages of sleeping sickness. The total number of cases in Europeans which have come under observation is now 50,[3] in which is included the present case. The present case is the first, so far as the writer knows, which has come under continued observation in America.

Is the Disease Curable? It is now generally agreed that cases treated in the early stage (trypanosomatic stage) may recover, while those in the latter stage (sleeping stage) practically never recover. It is also recognized that the disease, like syphilis, is very chronic, with long periods of latency. Bearing in mind these facts, then, all conclusions with regard to cures should be taken with reservation until sufficient time has elapsed (placed by Todd[4] at eight years), and an adequate number of cases have been observed to make such conclusions reasonably certain.

Plan of Attack. Through the labors of Ehrlich,[5] the treatment of trypanosomiasis has been taken from the realm of empiricism to that of rationalism. While this rational treatment is far from conclusively proved, it offers the only intelligent plan of attack and defence in the fight against the trypanosome.

Underlying Therapeutic Principle. Drugs used in the treatment are studied with regard to their action upon the organism (organotropism) and upon the parasite (parasitropism). The fixation of the drug, by the chemoreceptors in the protoplasm of the parasite is the underlying principle of parasitropism, and upon this depends the efficiency of a drug in destroying the parasite.

The experimental evidence upon which this theory is proved is as follows: Drugs were found to be parasiticidal in varying degrees under different circumstances; thus, a drug which destroys the parasite in vitro may have no effect in vivo, and vice versa; or the effect may be both in vitro and in vivo; or there may be no effect under either circumstance.

All drugs then (with regard to their efficiency in destroying trypanosomes) fall under the following classification:

In Vitro.	In Vivo.
0	0
+	+
+	0
0	+

There is a fifth and very important, though as yet imperfectly understood, action. Here no changes either in morphology or motility take place in the parasite when subjected to the action of the drug in vitro, and no change in the course of the disease at first when the drug is introduced in vivo. Later, however, under

[3] Bagshawe, Bull. of the S. S. Bureau, 1910, ii, No. 20, 277.

[4] Archives of Internal Medicine, April 15, 1911, vii, No. 4, 500.

[5] Chemotherapie von Infektionskrankheiten, Zeitschr. f. ärztliche Fortbildung, 1909, vi, No. 23.

the influence of the drug, the disease terminates in complete recovery. This is supposed to be due to a destructive action upon the reproductive power of the parasite. By this destructive action, one generation only of parasites is capable of maintaining the pathological features of the disease, which disappears with the life of this barren generation.

Ehrlich's explanation of the first three in this classification, namely, the OO, ++, +O, is not difficult to understand. In the first there is no parasitropism under any circumstance. In the second, the parasitropism occurs under both conditions and the organotropism is not in excess of the parasitropism. In the third, the organotropism is in such excess of the parasitropism that the drug in vivo is valueless. For example, methylene blue has an organotropism five hundred times in excess of the parasitropism —that is to say, although there are chemoreceptors in the parasite (spirochetæ of relapsing fever) for methylene blue, these are rendered of too little value owing to the great excess of the organotropism.

The O+ is somewhat more complex. To this class belongs one of the most efficient of the drugs, namely atoxyl. It is, therefore, important to understand why in vitro it has no parasitropism, while in vivo it is more active. This paradoxical or indirect action is explained by Ehrlich as follows: Such drugs find no chemoreceptors in the parasite in vivo. When, however, they are introduced into the organism, they undergo a chemical change into another compound which in the case of atoxyl is probably paramidophenylarsenoxyd. In the latter the arsenic molecule is unsaturated and the additional affinities enable it to combine chemically, while the arsenic molecule in atoxyl has no such additional affinities and the drug is therefore inert.

The arsenic receptor of the trypanosome is adapted not to pentavalent (atoxyl) but to trivalent arsenic (paramidphenylarsenoxyd). The drugs, therefore, which concern us clinically in the treatment of trypanosomiasis are those belonging to the ++ and the O+ class.

Available Drugs. In the laboratory several hundred drugs have been experimented with, but the following are some of those which have been tested out clinically, and from these certain ones were selected for the treatment of the case here reported.

1. The arsenic and antimony group:

Arsenic: (*a*) arsenous acid; (*b*) atoxyl, arsacetin, etc.; (*c*) acetylatoxyl; (*d*) arsenophenylglycin; (*e*) salvarsan.

Antimony: (*a*) Metallic antimony; (*b*) antimony sodio and potassium tartrate; (*c*) aneline antimony tartrate; (*d*) antimonytheoglycolic acid compounds.

2. Azo dyes group: (*a*) Trypan red; (*b*) trypan blue; (*c*) trypan violet.

3. Basic triphenylmethane dyes group: (*a*) Parafuchsin; (*b*) pyronin; (*c*) trypanosan.

Choice of a Drug. In selecting a drug, the stage of the disease and treatment previously employed must be taken into consideration.

In the early stage atoxyl (O+) is accepted at present as *the* drug. (1) Should atoxyl be used in the early stage only? or (2) should it be used for a period and replaced by another drug to be again used for a period ("ringing the changes," as Todd[6] well expresses it)? or (3) should the drug be continued, in small doses, for long periods irrespective of the course of the disease? In the continued use of this or any arsenic compound, animal experiments have shown that the great danger is that there may develop a generation of trypanosomes with resistance to arsenic (resistant strains). With regard to this, the authorities differ—Ehrlich cautions against the danger, pointing out that a case of trypanosomiasis with a resistant strain of parasites is worse off than one on whom no treatment has been instituted. Manson,[7] who has had a large percentage of recoveries, advises, on the other hand, the continued administration of small doses of arsenic. He says: "I would therefore suggest for the routine treatment of trypanosomiasis a 2- to 3-grain dose of atoxyl every second or third day and kept up for *at least two years.*"[8] According to the laboratory studies the development of resistant strains renders the trypanosomes invulnerable to almost all drugs. Perhaps the safest plan is to procure from time to time specimens of blood from a patient under arsenic treatment and by animal inoculation determine whether trypanosomes, resistant to the drug, are present. Closely allied to this consideration is the hypersensitiveness to ordinarily harmless doses of other drugs, acquired by one who has been taking certain preparations over a considerable period. Thus Ehrlich[9] warns against the toxic effect of even small doses of arsenphenylglycin upon one who has been under atoxyl treatment.

Dosage. Regarding the dosage, it must be remembered that the drugs employed belong to a highly toxic class, and that in their behavior they are as deadly as the disease; no drug, except in desperate cases, whose efficient dose is eight- to nine-tenths the lethal dose should be employed. The danger is too great. This danger is, however, offset by the fact that it is rarely necessary to increase the dose if once the quantity necessary to destroy the parasites is determined. This is true of antimony especially. Plimmer,[10] in speaking of intramuscular injections of antimony, advises against "pushing the dosage."

[6] Private correspondence.
[7] Loc. cit.
[8] Italics not in original.
[9] Private correspondence.
[10] Private correspondence.

On the other hand, a dose (of arsenophenylglycin) too small to destroy the parasites will not become efficient by allowing intermissions between the doses. On the contrary, the trypanosomes will develop resistance and the body will become hypersensitive. This intermittent treatment with small dosage is, therefore, condemned by Ehrlich as ineffectual and tending to produce resistant strains and body hypersensitiveness.

Summary. When the views of the authorities are summed up, we are led to conclude as follows:[11] The arsenic and antimony group of drugs offers the best ammunition with which to attack the trypanosome in the early stage of the disease. An exact dose should be ascertained by observing what quantity of a drug is necessary to rid the blood of parasites. Once this is found, no more and no less should be given. Treatment, with some parasiticide, should be continuous. No drug should be continued for too long a time, but frequent changes should be made (see below).

I add the opinion of Manson,[12] who has treated 10 cases in Europeans, with 3 deaths and 7 "apparently well," the case here reported being one of the 7. He says: "I am a believer in small doses of antitrypanosomiasis drugs—at least the arsenic and the antimony ones—considering that a persistently unfavorable[13] medicine is of more use than an intermittently unfavorable one." And again: "I do not believe we can kill the trypanosome outright by one or two large doses of atoxyl any more than we can kill the treponema of syphilis or the parasite of malaria by large doses of their respective specifics. Mercury does not immediately cure syphilis, nor does quinine immediately cure malaria; but they deprive the respective parasites of their pathogenic qualities and keep the patient alive and in good health until, in process of time, the parasites either die out or become permanently inert. So I read the action of atoxyl in traypanosomiasis, and so I would regulate its administration, being careful, as we would with mercury or quinine, not to push the drug too far, and thereby necessitate its suspension."[14]

The development and maintenance of the body resistance is placed by many authorities among the most important requisites. Thus Bagshawe[15] says recovery "may be attributed to the resisting power of the human organism at least as much as to the treatment." Manson[16] says: "I regard a high level of general health as of the utmost importance in the management of these cases." Again Manson[17] says: "The patient should be brought home to his

[11] For a good summary of Ehrlich's views see the Chemotherapy of Ehrlich, with Special Reference to the Trypanosome Injections, B. T. Terry, M.D., Medical Record, New York, April 8, 1911.

[12] Private correspondence.

[13] "Unfavorable" to the life and development of the parasite.

[14] Loc. cit.

[15] Loc. cit.

[16] Private correspondence.

[17] Loc. cit.

native country, be spared fatigue, worry, exposure, excess of all kinds, and be placed in the most favorable hygienic conditions possible."

Clinical Report. Before presenting the clinical findings in detail, I will give here a complete list of the symptoms and signs so far recorded in all cases, arranged according to their presence or absence in the case here under consideration:

Present in this Case.	Not Present in this Case.
Stinging sensation upon some exposed body surface. On hand in this case; thought at time to have been prick of thorn; no painful swelling followed.	Loss of weight and strength.
Fever.	Edema.
Erythema of skin.	Anemia.
Enlarged cervical glands.	Enlarged liver.
Itching of arms, legs, and body.	Epistaxis.
Large spleen.	Diarrhea.
Vomiting.	Delirium.
Loss of hair (scalp).	Tremors.
Headache.	Eye symptoms.
Insomnia.	Deafness.
Inertia—not loss of strength, but profound disinclination to mental or physical effort.	Phlebitis.
Depression. Melancholia, at times profound.	Orchitis.
Hyperesthesia, deep (Kerandel's sign).	Incontinence (urine and feces).
Severe aching in legs.	Dermatographia.
Loss of weight (temporary).	Paresthesias.
Pain in extremities; legs only in this case.	Vertigo.
Pain in long bones.	Changes in character.
	Facial paralysis.
	Epileptic seizures.
	Somnolence.
	Delusions.

As already stated, the findings from June 22, 1907, to December 12, 1907, in this case have been published by Manson[18] and Bagshawe,[19] and I quote here from the former's report:

"An engineer, aged thirty-five years, arrived at Boma, Congo River, on June 22, 1907. He was then in perfect health, and proceeded at once up country to a point about one hundred and fifty miles above Stanley Pool, where he and his companions camped on the river bank from June 28 until July 17. Four days after his arrival there he began to ail with anorexia, depression, languor, drowsiness, and on July 12 took to his bed with fever (102°). On July 17 his temperature had reached 107°. Next day he was brought to Leopoldville (fever, 104°), and on the following day, July 19, Dr. Broden found trypanosomes in his blood. He received a large dose (I understand 1.5 grams) of atoxyl hypodermically on the 20th. This gave rise to violent gastralgia, but on the 21st his temperature had become normal and has remained so ever since, with the exception of slight brief rises (99.5° to 102.4°), which recurred with some regularity every fortnight or three weeks. On July 23 daily injections of 0.25 gram of atoxyl were commenced and, with occasional intermissions of a day or two and increases of the dose

[18] Loc. cit.

[19] Loc. cit.

to 0.5 gram, were continued until his arrival in Liverpool about the middle of October, 1907.

"Trypanosomes were unusually persistent in the peripheral blood in this case. Dr. Broden found them when the patient was at Leopoldville every time he looked for them. Dr. Breinl, who examined him on his arrival in Liverpool, found them, notwithstanding intensive doses of atoxyl, on each of five successive days; and I found them whenever I examined the blood—that is, on every alternate day—between October 23 and November 8. When I saw the patient for the first time on October 23, he informed me that he had no cutaneous eruption, and that only once—during the initial fever, when one slightly enlarged gland was detected on the right side of the neck—any adenitis. An inflamed patch of skin on the dorsum of the right foot, which began on September 20, and which he attributed to prickly heat, had almost disappeared when I saw him. The spleen was slightly enlarged, and he looked more anemic than his blood count (4,000,000) indicated. Appetite was poor and he felt weak and depressed. There was no palpitation or breathlessness, and no headache even when he had fever. The only pain he remembered was intense aching in the legs, coming on every night and keeping him from sleeping; this disappeared when he left Leopoldville, and has not recurred.

"On November 8, trypanosomes being present in small numbers in his blood and temperature being normal, for the first time during his illness the characteristic erythema showed itself on the skin of the trunk. At the same time and for a day or two previously he had been profoundly melancholic, so much so that I feared the nervous system was becoming implicated and that the terminal phase of the infection was about to set in. He was so depressed that I was afraid to let him go out alone. On the day the erythema appeared (November 8) I gave him a hypodermic injection of $\frac{1}{2}$ grain of sodio tartrate of antimony, and also on the following days 1, $1\frac{1}{2}$, 2, and 3 grains respectively, and again after two days another 2 grains. The apparent effect of these injections was remarkable. By the third day the erythema had disappeared, his spirits had become good, and for the first time trypanosomes could not be found in his blood. This hopeful condition persisted until November 26, when depression, though not so intense as on the former occasion, returned and trypanosomes in greater number than I recollect to have seen them in human blood were once more found. On November 26 and 27 he had 2 grains of antimony by the mouth. I was afraid to resume the antimony injections on account of the intense irritation and pain they gave rise to. Given by the mouth the drug caused nausea and seemed to increase the depression. It was stopped, therefore, and atoxyl resumed. By the 30th trypanosomes had again disappeared and the patient was feeling much better. He left for New York on December 12, with instructions to continue the atoxyl."

To this record of Sir Patrick Manson I would add the following:

Five or ten days before the initial fever the patient experienced a sharp, stinging sensation on his hand, which he thought due to a prick of a thorn. There was no swelling or local redness. I wish to draw attention also (see temperature chart) to the character of the fever from November 9 to December 9, 1907, associated with and following the hypodermic injections of antimony. This fever is almost a counterpart of that occurring from January 1 to 24, 1909 (see temperature chart), when intramuscular injections of antimony were given. These two fever periods should be compared with the trypanosomatic febrile paroxysms and that associated with the intravenous injections of antimony (see temperature chart for February 1 to 15, 1910), to be described in detail later.

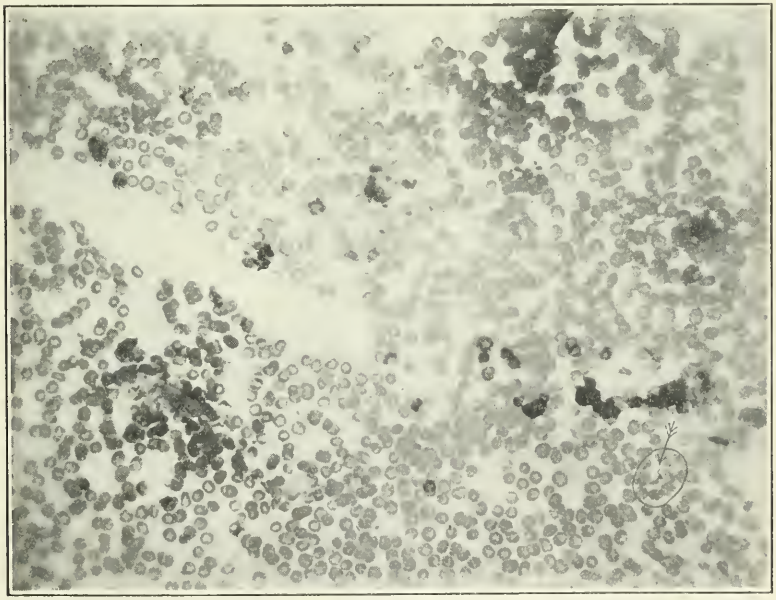

FIG. 1.—Trypanosoma gambiense, as observed in this case. Note relative size and number of erythrocytes to parasites. (Photograph by Dr. Auchincloss.)

I saw the patient for the first time on December 26, 1907. At that time he was in good spirits, energetic, but rather pale; the anterior and posterior cervical glands were palpable, and about the size of a pea; also the axillary glands, which were about the size of an almond; they were not tender. The epitrochlear glands were not palpable, though there was a history of lues which had received active treatment. There was some periosteal thickening of the shin bones, but no tenderness. The skin was clean but very dry and scaly, which he says at night becomes red and itchy, especially over

the shins. The swellings caused by the hypodermic injections of antimony (given November 9, 10, 11, 12, 13, and 14, 1907) were still present. Blood was negative for trypanosomes. Hemoglobin, 90 per cent. The spleen was not palpable.

January 8, 1908. Last evening he spent at my house; he was perfectly well then. Today he has a temperature of 102.4°. This paroxysm of fever is the fifth since date of infection (see temperature chart, paroxysm V). Blood shows abundance of trypanosomes —parasites found in about fifteen minutes (see Figs. 1 and 2).

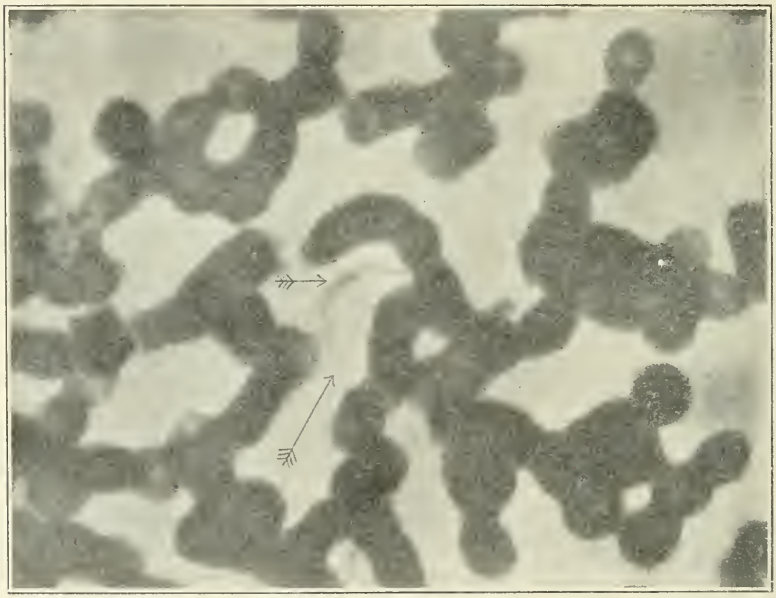

FIG. 2.—Trypanosoma gambiense, as observed in this case. Note the flagellum (long arrow) and nucleus proper (short arrow). The undulating membrane and micronucleus cannot be seen. (Photograph by Dr. Auchincloss.)

January 9, 1908. Trypanosomes absent—5 white rats inoculated with blood.

January 30, 1908. Large patch of erythema on thigh and abdomen.

March 16, 1908. VI. Paroxysm of fever (see temperature chart); nausea, bone pains, and debility.

April 14, 1908. VII. Paroxysm of fever (see temperature chart); trypanosomes present, nausea, vomiting, pains in legs.

April 27, 1908. VIII. Paroxysm of fever (see temperature chart); nausea, pains in legs, depression,

May 19, 1908. Deep hyperesthesia over superficial bones (Kerandel's sign).

May 25, 1908. IX. Paroxysm of fever (see temperature chart),

June 9, 1908. X. Paroxysm of fever (see temperature chart); great depression and weakness.

June 25, 1908. XI. Paroxysm of fever (see temperature chart); great depression and weakness.

July 3, 1908. XII. Paroxysm of fever (see temperature chart); great depression and weakness.

From July 12, 1908, to November 22, 1908, there was irregular and continued fever with no marked paroxysm (see temperature chart). During most of this time the patient was feeling well. He had slight depression and occasional nausea when temperature reached 99°, which it did six times. On three occasions it reached 100°. Thus, in three and one-half months temperature was above normal nine times, but not above 100° (see temperature chart). During August and September patient was in the Canadian woods. His weight steadily increased, coming from 154½ pounds (March 3, 1908) to 161 pounds (October 24, 1908).

November 24, 1908. XIII. Paroxysm of fever (see temperature chart).

November 28, 1908. Trypanosomes absent. Cervical glands punctured. Trypanosomes absent (examined by Dr. J. L. Todd). Two rats inoculated with blood and glandular fluid.

December 3, 1908. XIV. Paroxysm of fever (see temperature chart); nausea and depression.

December 10, 1908. Trypanosomes present.

December 12, 1908. Blood viscosity; 7.7 times water (5.1 normal) (Hastings). Blood osmic tension, water value, 45.9; blood value, 46 (Hastings). Blood alkalinity; Fl. 0.380 in NaOH per 100; disod. perc., 0.020.

Treatment (from December 9, 1907, to December 6, 1908. Atoxyl hypodermically). Atoxyl, 3 grains hypodermically administered every other day, was the only medicinal treatment during this period of one year. On November 24 and December 3, 1908, there were sharp paroxysms of fever (see temperature chart), with nausea and depression; and on December 12, 1908, trypanosomes were present in the blood. The cervical glands were, however, free from trypanosomes. Fevers following one another in such quick succession and the presence of trypanosomes were decidedly unfavorable signs. Coming, too, after a period of six months of general improvement, which was associated, however, with irregular fever, caused anxiety lest a generation of atoxyl-fast parasites had developed.

December 6, 1908, to December 22, 1908 (arsacetin hypodermically). Brief trial of arsacetin was made, but on December 22 all arsenic medication was discontinued. On this date the blood showed a red cell value of 5,200,000; hemoglobin, 85 per cent.; color index, 0.83; white blood cells, 8000, with a slight polymorphonuclear increase.

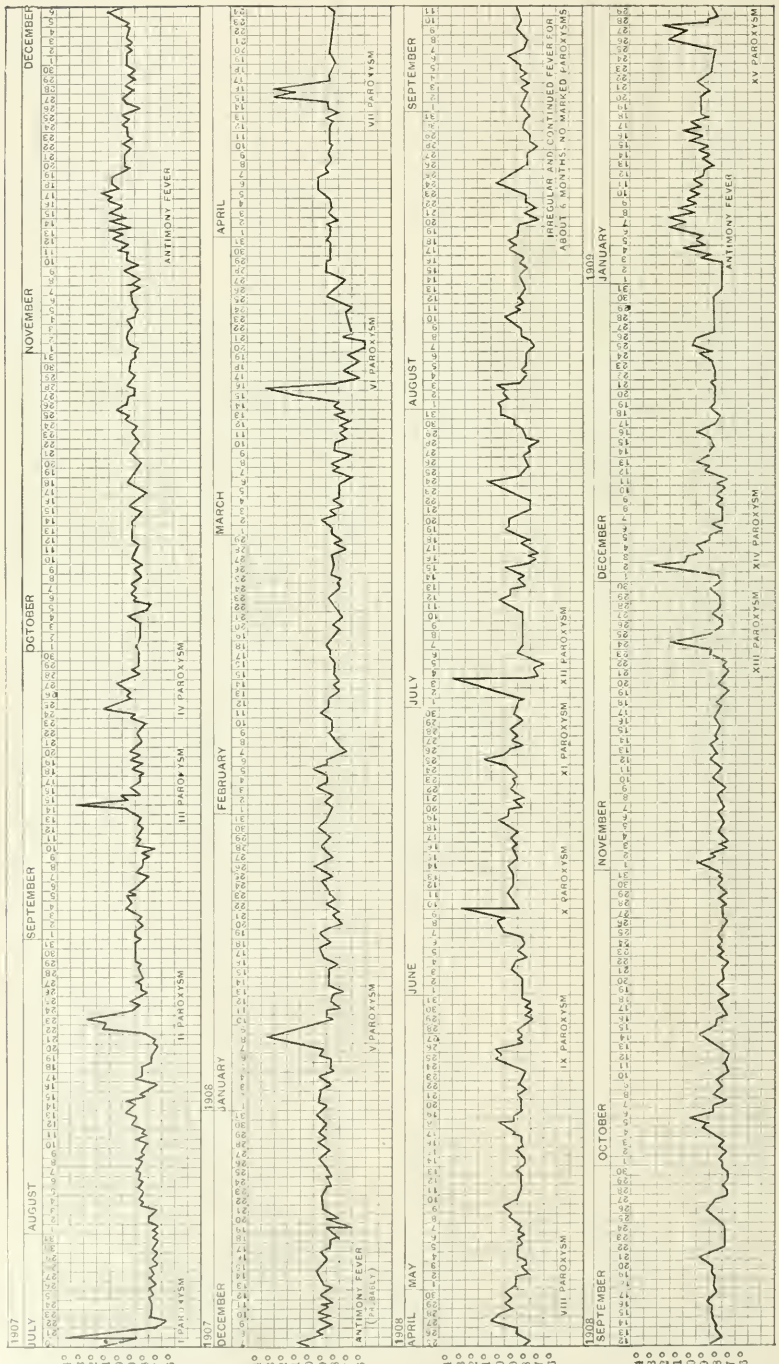
1907
JULY
AUGUST
SEPTEMBER
OCTOBER
NOVEMBER
DECEMBER
I PAROXYSM
II PAROXYSM
III PAROXYSM
IV PAROXYSM
ANTIMONY FEVER
1908
JANUARY
FEBRUARY
MARCH
APRIL
ANTIMONY FEVER (PASSAGE)
V PAROXYSM
VI PAROXYSM
VII PAROXYSM
1908
APRIL
MAY
JUNE
JULY
AUGUST
SEPTEMBER
VIII PAROXYSM
IX PAROXYSM
X PAROXYSM
XI PAROXYSM
XII PAROXYSM
IRREGULAR AND CONTINUED FEVER FOR ABOUT 6 MONTHS, NO MARKED PAROXYSMS
1908
SEPTEMBER
OCTOBER
NOVEMBER
DECEMBER
1909
JANUARY
XIII PAROXYSM
XIV PAROXYSM
ANTIMONY FEVER
XV PAROXYSM
104°
103°
102°
101°
100°
99°
98°
97°
96°

FIG. 3.—*Temperature Chart.* Continuous record of temperature from date of infection, June, 1907, to date of disappearance of fever, March, 1910, two years and ten months. Antimony fevers occurred November, 1907, January, 1909, and February, 1910. Trypanosome fevers numbered twenty-six. The last fever attributable to trypanosomes occurred November 9, 1909. Last fever of any origin occurred February 14, 1910. In the text will be found a record of the clinical features and treatment employed in connection with each of the febrile phases represented in above chart.

Antimony medication was now seriously considered, but no preparation sufficiently safe could be procured in this country for intramuscular and intravenous injection. From Messrs. Larimore & Co. a solution of antimony lithium tartrate, prepared with great care, was procured for administration by mouth.

December 16, 1908 (antimony lithium tartrate by mouth). One and one-half grains of this preparation in three pints of water was taken by mouth daily. About this date Sir Patrick Manson was cabled to, and from him two preparations of antimony were received.

January 3, 1909 (precipitated metallic antimony intramuscularly). On this date 10 minims, equal to one-half grain, of precipitated metallic antimony in Lambkin's oily medium was injected into the muscles of the buttock. This preparation was the identical one which had been tested by Plimmer in the treatment of syphilis in one of the British military hospitals.

Within an hour after the injection the patient experienced in the buttock great discomfort, which increased until the whole buttock was greatly swollen, painful, and tender, to such a degree that the least pressure of his body upon the bed caused him to call out with pain. Even with such cause removed, the pain was so intense that morphine had to be frequently administered. This condition, accompanied with sleeplessness, lasted for ten days, when the swelling, pain, and tenderness gradually subsided, and within a fortnight from date of injection the patient was able to walk about, and two days later all inconveniences had disappeared. When the area of swelling had lost the tenderness sufficiently to allow of palpation, it was found to be tense, hard, and fairly sharply defined to a circular area of about 18 to 20 cm. in diameter. There was no necrosis. The temperature was as is shown in the accompanying chart (see temperature chart of January 3, 1909).[20]

The temperature curve during this period seems to be quite characteristic when compared with that of November 9, 1907, at which date antimony was given hypodermically.

In speaking of his results with this identical preparation, Plimmer[21] says: "In the cases at Millbank none of the men had to lay up, not even after 20 minims, and the pain lasted only a few days and none suppurated," and Manson[22] says: "It may be injected once every one, two, three, or four weeks. The maximum dose hitherto used has been 20 minims (it is a 5 per cent. mixture), equal to 1 grain. They begin with 10 minims; . . . a little local irritation may follow."

Janurary 14, 1909 (antimony by mouth). Antimony sodio tartrate, which had been discontinued on January 4, 1909, owing to his condition, was on this date again taken by mouth in amounts of $1\frac{1}{2}$ grains in 3 pints of water daily. The urine was negative.

[20] Camac, Amer. Jour. Med. Sci., August, 1911.

[21] Private correspondence.

[22] Private correspondence.

January 27, 1909. XV. Paroxysm of fever (see temperature chart); marked depression. Condition of patient now seemed very unfavorable. Though there were no trypanosomes in the blood and rats inoculated with the blood and cervical gland fluid were negative, there was apparently a resistance to atoxyl. Intramuscular injection of antimony was out of the question.

January 28, 1909, to February 18, 1909 (atoxyl hypodermically). Sir Patrick Manson's advice to continue small doses of atoxyl for "at least two years" and his good results in so doing seemed to justify resuming the atoxyl hypodermically. This was done, three grains being given thrice weekly. Antimony by mouth daily also was given. Irregular fever continued for about one month.

February 18, 1909 (antimony intravenously). On this date $\frac{1}{8}$ grain of antimony sodio tartrate in normal saline was injected into the vein of the arm. This preparation also was received from Sir Patrick Manson and Mr. Plimmer, as mentioned above. Atoxyl was discontinued on February 17, 1909, but the antimony by mouth daily was continued.

February 25, 1909. One-quarter grain antimony sodio tartrate intravenously injected. Urine negative.

On March 4, 9, 13, 18, 23, 27, 1909 (that on the last date being the eighth injection), he had $\frac{1}{8}$ grain antimony sodio tartrate injected intravenously. Negative findings in urine.

March 27, 1909. XVI. Paroxysm of fever (see temperature chart).

April 6, 1909. One-quarter grain antimony sodio tartrate, intravenously injected.

April 6, 1909. XVII. Paroxysm of fever (see temperature chart).

April 12, 1909. One-eighth grain antimony sodio tartrate intravenously injected.

April 17, 1909. One-sixth grain antimony sodio tartrate, intravenously injected (being the twelfth injection).

April 19, 1909. Atoxyl, 3 grains hypodermically begun and taken thrice weekly until October 30, 1909.

April 28, 1909. XIX. Paroxysm of fever (see temperature chart).

May 4, 1909. Antimony by mouth discontinued.

From May 1, 1909, to July 14, 1909. Patient left for Western States and the Canadian Northwest. Headache constant, not severe; sleep much disturbed; no fevers.

July 14, 1909. XX. Paroxysm of fever (see temperature chart).

July 29, 1909. XXI. Paroxysm of fever (see temperature chart). Weight, 156 pounds.

August 16, 1909. Erythema on right leg, lasting about a month.

August 28, 1909. XXII. Paroxysm of fever (see temperature chart).

September 13, 1909. XXIII. Paroxysm of fever (see temperature chart). Weight, 161 pounds.

October 9, 1909. Antimony lithium tartrate 1.5 to 2 grains in 3 pints of water by mouth daily.

October 13, 1909. XXIV. Paroxysm of fever (see temperature chart).

October 25, 1909. XXV. Paroxysm of fever (see temperature chart).

October 30, 1909. Atoxyl discontinued.

November 1, 1909. Returned to New York after a successful journey through the west. His condition was excellent and he had been fairly free from nausea, depression, sleeplessness, and headache. The fevers were, however, quite severe and frequent (see temperature chart). It was therefore determined to again give the antimony by the vein.

Arsenophenylglycin Considered. At this time arsenophenylglycin was considered and a preparation procured from the Rockefeller Institute from Dr. Flexner, who had received it from Professor Ehrlich. Upon the advice of Professor Ehrlich,[23] however, it was not used. He cautioned against using it after prolonged administration of other arsenic preparations (atoxyl) (see earlier portion of this paper for consideration of this action of arsenic compounds, p. 661).

November 9, 1909. XXVI. Paroxysm of fever (see temperature chart). *Last fever attributable to trypanosomes* Trypanosomes present in the blood. Two white rats inoculated with blood. One sent to Dr. Todd to test for atoxyl-fast trypanosomes.

Antimony Intravenous Injection. One-sixth grain antimony sodio tartrate intravenously injected. This injection was repeated November 15, December 2, 7, 13, 23, 28, January 3, 10, 15, 25, and February 1, 1910, about 11 A.M. About twenty minutes after leaving the laboratory, while on his way home, the patient was suddenly seized with nausea and great weakness. He managed to reach his home unaided. Before I could get to him he had had a chill and violent abdominal pain. When I saw him he was greatly prostrated, complained of intense headache, and had a temperature of 103.6° (see temperature chart). This lasted five or six hours, subsiding to normal. The blood was negative for trypanosomes. The urine showed great excess of indican, otherwise it was normal. For twelve days the weakness and abdominal distress continued, and on the thirteenth day from the former paroxysm he had, for six hours, a similar but somewhat less severe attack (see temperature chart). Trypanosomes were not found at the time of this second fever and *have been absent upon all subsequent examinations.*

[23] Private correspondence.

The temperature curve presents very different characteristics from that of either the intramuscular or hypodermic injections of antimony (see temperature charts of November, 1907, and January, 1909), though there is some similarity to that of the trypanosome fever. No trypanosomes, however, were found in the blood with either of these rises in temperature.

The behavior of the disease subsequent to these alarming manifestations of what would seem to be antimony poisoning is most important. The last fever due to trypanosomes occurred November 9, 1909, just before the first of the second series of intravenous injections of antimony. This fever was paroxysm XXVI since the beginning of the infection. These twenty-six paroxysms of fever occurred over a period of two and one-half years (June, 1907, to November, 1909). With these fevers trypanosomes almost invariably were found in the peripheral blood. Except for the two fevers following the antimony (poisoning?) injections no fevers have occurred to date, October, 1911, nearly two years, and trypanosomes have not been found in the blood. For a few months atoxyl was resumed for its tonic effect, and then all trypanosomatic medication was discontinued.

April 14, 1911. A monkey (Rhesus) and a rat were inoculated, intraperitoneally, with peripheral blood. Also a monkey (Rhesus) and a mouse with spinal fluid. These animals have remained normal to date, October, 1911. The direct examination of the blood and spinal fluid was negative for trypanosomes.

The patient has engaged in some business undertakings; he finds himself, however, easily depressed by ordinary business reverses. This depression has at times been of rather a serious grade, and he cannot stand oppressive summer heat. With these exceptions there are no other abnormal manifestations.

Conclusions. As remarked at the beginning of this communication, sufficient time has not elapsed since trypanosomiasis was definitely known to be an early stage of sleeping sickness, in which to determine the duration of this disease.

Bagshawe's[24] summary of the 50 cases in Europeans so far recorded gives the following: "30 are known to be dead, 11 survive, and the fate of the remaining 9 is uncertain. Of the 30, 14 lived a year or more after trypanosomes were discovered and 4 two years or more. Of these, 1 lived three and one-quarter years, and 1 six years. . . . The fact that, of the 30 patients who died, 4 survived more than two years after the disease was diagnosticated, suggests that in cases which have exceeded this duration there is good hope of ultimate recovery."

The case here recorded now survives more than four years after the disease was diagnosticated.

[24] Case X of Bagshawe's series, loc. cit.

The case, mentioned above, who died six years after the diagnosis was made is quite exceptional and should be studied with due regard to all the peculiar features of the case. Todd, however, places eight years as the time limit in which a cure may be assumed.

Further criteria by which to determine whether the trypanosome is still actively present are to be found in animal inoculation. Todd gives one hundred and fifty days as the longest period in which monkeys infected with trypanosoma gambiense have remained free of symptoms. Rats usually die within a month, but three hundred and eighty-eight days is the longest time recorded without symptoms.

The record of this case is now published to date in order that it may be placed within reach of those studying the disease, but all conclusions upon the question of cure are reserved until sufficient time has elapsed to make such conclusions of value.

When this case first came under my care I was quite unfamiliar with the disease and its treatment; I have therefore many acknowledgments to make for assistance received from various sources. The antimony administrations were carried out with the assistance of Professor T. W. Hastings, of the Cornell Clinical Laboratory, who rendered me valuable aid in other respects also. From Sir Patrick Manson I have received, through correspondence, advice without which it would have been impossible to deal with so insidious a disease and with such treacherous drugs.

In the autumn of 1908 the patient and I consulted Professor J. L. Todd, in Montreal, who offered suggestions, and who made examinations already referred to. I want also to thank Drs. Terry and Cole, of the Rockefeller Institute and Hospital, for their assistance in the animal inoculations.

EXPERIENCE WITH PULMONARY TUBERCULOSIS DURING THE LAST YEAR.[1]

A CLINICAL RÉSUMÉ.

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During recent years there has taken place a world-wide agitation toward the suppression and control of tuberculosis. Laboratory research has been stimulated and a vast amount of laborious scientific work performed. An elaborate organization for the campaign

[1] Read before the National Association for the Study and Prevention of Tuberculosis, June 20, 1911.

has been perfected and innumerable associations for the study and prevention of tuberculosis have been formed. Detailed investigations pertaining to sociological and economical features have been completed and interesting conclusions reported.

An important phase of the tuberculosis movement has been the educational propaganda calculated, not only to awaken general attention but to instill into the public mind essential features of prophylaxis. The interest of the masses has been aroused through the medium of antituberculosis societies, public lectures, exhibitions, and the wide distribution of tuberculosis literature. In many communities effective results have been attained through the enactment of wise municipal ordinances and their rigid enforcement by capable administrative authorities. It may be safely assumed that much good has already been accomplished, as shown by the diminished mortality rate in a few of the larger cities. Apparently the greatest progress has been made in the cause of prophylaxis as reflected in the improved hygienic conditions of the home, workshop, school rooms, and other public buildings. It may be questioned if in the actual management of the disease, a corresponding advance has been achieved, although the comfort of many pulmonary invalids has been promoted by refuge in various institutions for hopeless cases.

A very considerable enthusiasm has been exhibited regarding new methods for the recognition of tuberculosis and the advantages of the sanatorium. A growing tendency has developed toward refinements of diagnosis and conventionalities of treatment. In the midst of the popular awakening as to the necessity of prophylactic measures, and the prevailing effort of medical advisers toward diagnostic proficiency, it is well to review certain clinical aspects of the tuberculosis movement. It is impossible in this connection to discuss the significance of rational symptoms or the varying interpretation of physical signs. Neither is it designed to elaborate details of hygienic and dietetic management. While correct conclusions as to the relative merits of the sanatorium and judicious climatic change are not always entertained, it is of present interest merely to note recent tendencies of the profession in its advisory capacity concerning a class of people requiring most competent direction.

Are pulmonary invalids today profiting by early diagnosis, conservatism of management and stability of judgment to a greater extent than a decade ago? It is possible that some information may be afforded by the experience of medical observers in various health resorts. Exceptional opportunities for a comparative clinical study of all classes are given to physicians residing in regions possessing climates so favorable as to attract patients from all sections and from long distances. This is particularly true of clinicians unattached to closed institutions which enforce rigid entrance restric-

tions. In the hope of presenting data which may prove of interest and reflect, perhaps, to some extent, the attitude of other medical observers, reference will be made to a few general and statistical observations. The results are based upon a personal experience during the past nineteen years in the supervision of over 3000 private cases of pulmonary tuberculosis the records of which have been preserved.

The unavoidable limitations and deficiencies of statistical contributions are well known. Sources of error, however, have been eliminated as far as possible and much labor expended to render the analysis accurate and simple. In a clinical retrospect of this character it is obviously appropriate to introduce only such material as may have practical significance, and permit reasonable conclusions with reference to certain important phases of the general subject.

In my earlier experience in Colorado ample opportunities were afforded to note the unfortunate results of delayed diagnosis. In most instances a comprehensive review of the history and subjective symptoms together with thorough physical and bacteriological examinations, would have sufficed to establish a much earlier recognition of the disease. While the more recent means of diagnosis were not at that time available, intelligent recourse to the old-fashioned methods would, to a great extent have prevented disastrous delay.

It was found from a compilation of statistics made some years ago that the average period of delay in 2300 patients before arrival in Colorado was eighteen months. Notwithstanding the diversified character of cases, and the relatively large proportion of those in moderately and far advanced stages, the results obtained upon the whole, were of such a nature as to dispel any possible doubt as to the advantages accruing from a wisely directed climatic change. Instances of mistaken diagnosis were then comparatively infrequent. While patients were found from time to time to have been instructed injudiciously the difficulties of subsequent management were not pronounced. Invalids, as a rule, did not entertain preconceived notions as to their individual needs, and hence were usually amenable to advice and supervision. They were duly impressed with the possible gravity of their condition and had not imbibed an idea as to the curability of tuberculosis at home. A large majority of the patients were sent away directly upon the advice of the family physician.

In November, 1909, in a paper embodying the study of 313 pulmonary invalids coming under observation since the publication of other statistics, some data were submitted suggesting changing tendencies of the profession in the diagnosis and management of tuberculosis. An interesting feature was the surprisingly large number sent to Colorado upon a mere suspicion of tuberculosis.

In ninety instances, or more than one-quarter of the cases presenting themselves for examination, the physical exploration of the chest was entirely negative, while tubercle bacilli were unrecognized in the sputum in 87. They were occasionally found, even in the absence of physical evidence of tuberculosis, and the reverse was also true in some instances. "Of the doubtful cases without either physical or bacteriological evidences of infection the tuberculin test was negative in 41." Although in 87 cases the period of indisposition had lasted merely from two weeks to four months, the average period of delay for the entire number was found to be sixteen and one-quarter months, thus corresponding rather closely with previous observations. One hundred and twenty-five, or nearly two-fifths were found to be in advanced stages, 62 dying not long after arrival, and 16 being sent home as utterly hopeless. With 90 classed as doubtful, including 41 adjudged non-tuberculous, and with 125 as very advanced, a comparatively small number were found to exhibit an infection of incipient or moderate degree. Comment was then made upon the fact that despite a positive cutaneous reaction, a definite diagnosis of an active tuberculous involvement was often subject to some doubt. While a very considerable number of such cases were thus impelled to journey long distances, many clearly tuberculous patients exhibited complications of such a nature as properly to have contraindicated their departure, persisting albuminuria being present in 25 instances, an incurable infection of the larynx in 15, and intestinal tuberculosis in 7. A typical pneumonic onset was exhibited in 19, the disease pursuing the characteristic course of acute pneumonic phthisis in 12. Cardiac dilatation was occasionally observed, dyspnea from various causes not being infrequent.

As a result of this analysis, two central thoughts were suggested. (1) It appeared that attempted over-niceties of diagnosis sometimes resulted in the incorrect interpretation of physical signs, a judicious discrimination not always being in evidence as to the relative importance of the various features. In the commendable zeal for early diagnosis it seemed that a source of error was found in our enthusiasm to recognize somewhat obscure physical evidences of infrequent occurrence and doubtful import. (2) It was apparent that in advanced cases, faith in the efficacy of the home treatment and in the advantages of local institutions were responsible to a degree for the disastrous delay, and hence in some cases, for the unfortunate condition of those seeking climatic aid as a last resort.

Attention was further called to the increased frequency with which tuberculin was administered as a routine procedure irrespective of modifying conditions. A source of some surprise was the frequency with which the mercury treatment had been given. A stuffing process had been occasionally instituted, notwithstanding contraindications found in the digestion, circulation, or elimination.

A tendency was observed to minimize the importance of rest and to advocate less unreservedly the value to be derived from exercise not always within moderate bounds. Attention to the temperature and pulse apparently was not always a guide to the degree of physical exertion permitted.

There was convincing evidence to suggest that the necessity of strict obedience to hygienic precautions had been duly emphasized. Patients and accompanying members of the family were frequently found to have acquired a fund of knowledge as to the nature of the infection and the details of treatment. With many, particularly those of a judicial mind, the previous course of instruction was found to be of signal advantage. Others with unfortunate peculiarities of temperament and disposition were found altogether too familiar with the subject, in short, were over-educated to such an extent as to render them difficult of subsequent management. The resourceful control of the consumptive, which is a necessary preliminary to the control of the infection was not always easy, provided fixed ideas as to the value of remedial agents, and prejudices relative to various methods of procedure had previously been formed.

In view of these observations of a statistical and general character it has been of some interest to analyze my experience during the past year to ascertain if previous impressions are to be confirmed or modified.

During the twelve months ending November 1, 1910, 222 new patients having real or supposed tuberculous involvement have presented themselves for treatment, the large majority seeking medical counsel immediately upon arrival in Colorado. In addition there have been under supervision during the year, 80 who had been under previous observation, making a total of 302 consumptives furnishing material for further analysis. Of the 222 new patients, the physical and bacteriological findings were negative in 55. Several before arrival and subsequently responded positively to one of the integumental tests. A large proportion of these patients were influenced to leave home immediately upon the development of cough, elevation of temperature, slight loss of weight, general malaise or other suspicious symptoms, and in very many instances, even without the advice of a physician. Some presented the history of bronchitis of indefinite duration, asthma, emphysema, general debility, malaria, and neurasthenia. Symptoms suggestive of mixed infection were exhibited by 19 and corroborated by the bacteriological findings. Of these, 13 presented the history of one or more pulmonary hemorrhages, in none of which cases were tubercle bacilli discovered. The thought is conveyed that possibly hemoptysis among non-tuberculous invalids is more frequent than commonly supposed. Attention has previously been called to fairly numerous instances of pulmonary hemorrhage resulting from vicarious menstruation, purpura hemorrhagica, and circulatory

embarrassment incident to chronic bronchitis, emphysema and pneumoconiosis. Nearly all patients having one or more hemorrhages without definite evidences of tuberculous involvement presented the history of a sudden onset with chill, fever, cough, and expectoration. In a few cases the clinical course had been of so acute a type as to suggest the probability of an actual pneumonic process with a central or concealed area of involvement. In one or two cases a definite recognition of the pneumonic consolidation was obtained after arrival in Colorado.

Six patients were found to have developed tuberculosis in Colorado, 4 without apparent cause, 1 as a result of dissipation, and 1 following chronic bronchitis and pneumoconiosis.

Of the remaining 161 tuberculous patients coming during the year, the average period of delay before arrival was thirteen and one-half months, thus showing a gratifying change from previous years. More than 50 per cent. left home within six months after the onset of the disease. A large proportion of the balance had been to various health resorts for such prolonged periods as to increase the average delay for the entire number to thirteen and one-half months. It thus appears that the present tendency is for pulmonary invalids either to seek climatic relief or to avail themselves of institutional advantages somewhat earlier than in previous years. It is noted, however, that not infrequently early climatic change is found to have been directly opposed by attending physicians.

Thirty patients presented the history of a prolonged sojourn in institutions for consumptives. Of these 5 had exhibited satisfactory improvement, 4 had gained substantially and then relapsed, 2 exhibited no physical or bacteriological evidence of tuberculous infection, 1 of these having resided two years in a sanatorium, taking tuberculin during the entire period, and the other as often as every other day. Nineteen apparently failed to derive even temporary benefit and experienced as a result not only loss of time but of opportunity. Of these 1 had remained in an institution nineteen months, 1 two years, 2 had been in three sanatoria, and several in two. Of the thirty patients, 24 were far advanced, 2 incipient, and 2 without demonstrable tuberculous infection.

In the classification of patients, an effort has been made to conform strictly to the schema adopted by the The National Association for the Study and Prevention of Tuberculosis. In accordance with this grouping there were 27 incipient cases, 42 moderately advanced, and 92 far advanced. Attention has been called by writers to the enormous number of advanced consumptives sent to Western health resorts. It has been estimated that about 50 per cent. of the pulmonary invalids seeking climatic change are without the slightest possibility of cure in any region. This appears to be somewhat in line with my own observations, as of those with

demonstrable tuberculosis coming to Colorado during the past year nearly 56 per cent. were in very advanced stages, 26 per cent. moderately advanced, and but 16 per cent. truly incipient.

Further information is afforded by a study of the records with reference to the temperature, pulse, weight, and important complications. Of the 161 patients, statistical material is fairly complete in 150 cases. Of these, 108 exhibited a temperature of 100° or above at the time of arrival; 45, 101° or above; and 20, 102° or above. In 115 patients, the pulse was 100 or above, in 48, 110 or above, and in 37, 120 or above. The lack of correspondence between the physical signs and the pulse and temperature has been frequently noted. A number of patients classified as moderately advanced or far advanced have sometimes offered a relatively favorable prognosis upon the basis of but slight elevation of temperature, an excellent pulse, good appetite, and digestion. Others presenting the physical signs of incipient involvement have exhibited occasionally high fever, acceleration of pulse, nervous disturbances and important complications in addition to temperamental peculiarities and other conditions inimical to favorable results. The average loss of weight for the entire number before coming to Colorado was $20\frac{1}{2}$ pounds. The amount for the incipient class was $13\frac{1}{2}$ pounds, for the moderately advanced, 16 pounds, and for the far advanced, $24\frac{1}{2}$ pounds.

The following complications were observed: Tuberculous laryngitis in 20; tuberculous pharyngitis in 2; intestinal tuberculosis, not inclusive of fistula in 9; tuberculous peritonitis in 2; tuberculosis of the bladder in 2; tuberculosis of the kidney in 3; miliary tuberculosis of various types, 8; tuberculous glands, 1; perirectal abscess, 4; acute pneumonic phthisis, 5; pleurisy with effusion, 3; pneumothorax, 2; valvular cardiac lesions with varying degrees of compensation, 4; syphilis, 7; malaria, 5; diabetes, 2; advanced nephritis, 2; pregnancy at the time of arrival (far advanced case), 1. Albuminuria was noted in 61 patients. In many instances this consisted of a very slight trace sometimes undetected by the nitric acid test, but becoming definitely recognized by the heat test with acetic acid.

In attempting to estimate the results obtained among patients coming during the year, much difficulty is encountered by reason of the comparatively short period of observation, the extremely desperate condition and brief sojourn of a considerable number, the mixed character of the case, the differing circumstances, the not infrequent necessity of work, and for some the unavoidable absence of continuous supervision. Under these conditions it is possible only to form an approximate conclusion as to the degree and permanency of the benefits derived. In analyzing the results, however, a studious effort has been made to compile the statistics accurately.

It was not adjudged fair to include 35 patients remaining under observation but a very short time. Conforming strictly to the schema adopted by the The National Association for the Study and Prevention of Tuberculosis, it was found that of the remaining 126 irrespective of class, 29 did not improve, 30 improved, 34 were arrested, and 24 were apparently cured. None could be classed as actually cured on account of the shortness of time, two years without constitutional symptoms, physical or bacteriological evidences being required to permit inclusion in this classification.

Despite the diversified character of cases and the large predominance of those in far advanced stages, 77 per cent. have thus far exhibited degrees of improvement, nearly 35 per cent. being arrested cases, and nearly 20 per cent. apparently cured.

An analysis of results with reference to the several types shows that of the incipient cases, there were none who were not improved, 6 improved, 6 arrested, and 8 apparently cured. Of the moderately advanced, there were 4 unimproved, 5 improved, 13 arrested, and 11 apparently cured. Of the 3 classed as not improved, 2 had shown very pronounced gain in all respects until death resulted in one instance from aneurismal hemorrhage, and in the other from meningeal tuberculosis. The third was compelled to work daily in order to provide for the necessities of life for himself and family. Of the far advanced there were 26 unimproved, 19 improved, 24 arrested, 5 apparently cured, and 21 were either sent home or died very shortly after arrival.

Further information as to the progress made is acquired by a comparison of the gains established in body weight suggesting an increased resistance to the tuberculous infection. Of the far advanced cases who did not return home or succumb almost immediately, the average gain in weight was 9 pounds. Of those moderately advanced 14 pounds, only one in this group having failed to exhibit some improvement in this respect. Of the incipient cases, the average gain was 15 pounds.

Among 90 patients coming in previous years but remaining more or less under observation during the past twelve months, the results are grouped as follows: Not improved, 16; improved, 23; arrested, 32; apparently cured, 11; cured, 8. Of these the average gain in weight inclusive of those who did not survive, has been 16 pounds despite the fact that 8 failed to show any gain whatever. Of the 11 who died, 9 had gained materially in weight, as follows: 3, five pounds; 2, ten pounds; 2, thirty pounds; 1, twelve pounds; and 1, eight pounds.

Twenty-seven of the entire number observed during the year have died, a fatal termination being induced by exhaustion from advanced phthisis in 19, aneurismal hemorrhage (instantaneous) in 3, aspiration pneumonia following hemorrhage in 2, bronchopneumonia in 1, nephritis in 1, tuberculous meningitis in 1, intesti-

nal tuberculosis in 1, Schede operation in 1, pulmonary type of miliary tuberculosis in 3, and meningeal tuberculosis in 5.

The significance of the report as a whole is augmented by the fact that many were compelled to seek employment and were thus unable to conform to the régime in vogue in special institutions. Others were so handicapped financially as to preclude proper nourishment, and in some instances suitable accommodations.

A review of the foregoing statistical data serves but to accentuate previous impressions with reference to the early diagnosis and management of tuberculosis. From these studies, it seems reasonable to assume that while much has been accomplished in the past few years in the education of the public there is still something to be desired. It is to be expected that among different clinicians in varying localities, divergent views should be entertained according to the peculiarities of individual experience. In this instance, due significance must be attached to the number of persons sent away from home without positive evidence of tuberculosis, to the comparatively few early cases, the large proportion in moderately or far advanced stages, and the frequency of incurable complications. Opportunity has been permitted to note the disadvantages of routine tuberculin administration and the inevitable limitations of the sanatorium unless in a properly coördinated relation to other important measures of treatment. It is vitally important to recognize the value of a properly selected climate, the fundamental consideration being that of individual fitness. It is well known that notwithstanding a possible unhygienic environment and improper food and clothing, many incipient cases do recover at home, and that despite unfavorable climatic conditions, others somewhat more advanced, may exhibit periods of improvements while confined in closed sanatoria. While consumptives may recover in unsuitable regions, they are more likely to do so in localities wisely selected with reference to individual needs. In some instances, prompt recourse to a suitable climate represents the determining factor, but this is only capable of exerting its greatest influence when combined with a reasonable interpretation of modern hygienic and dietetic management. Experience has shown that many patients, who, through financial distress are deprived of the advantages of a supervisory régime, nevertheless are permitted to secure improvement amidst favorable climatic surroundings. To those compelled to work for a livelihood sojourn in a suitable locality may offer the only means of an eventual restoration of health. An arrest having been secured, a continued residence precludes in many instances, the relapse so common among individuals returning to their former occupations at home. In the interest of the consumptive class it is to be hoped that an increasing appreciation of the value of climate for properly selected cases may be justly entertained.

PERFORATION OF THE INTESTINES DUE TO TUBERCULOUS ULCERATION.

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Although intestinal ulceration is of frequent occurrence in chronic pulmonary tuberculosis, perforation of the intestine rarely happens. Cornet,[1] in his article on tuberculosis, says: "Eichhorst, in 462 autopsies on cases of pulmonary phthisis, found intestinal ulcers in 29.9 per cent.; Heinze, in 1226 cases of consumption, 51 per cent. of tuberculous disease of the gut; Honing, in 70 per cent.; according to other authors, they occur in 90 per cent. (Wright, Orth); Baumgarten found them rarely absent; Herxheimer observed them in 57 out of 58 cases of phthisis." Fenwick[2] found the intestine the seat of ulceration 500 times in 883 cases, or in about 56 per cent. I found, in going over 475 autopsies at the Phipps Institute, that the intestines showed ulcers in 313 cases, or in 65.9 per cent.

The frequency of intestinal perforation is given at figures varying from 5 per cent. (Willigk[3]) to less than 1 per cent. Fenwick, in 2000 autopsies, found that perforation of the intestine had occurred as the result of tuberculous ulceration in 25 cases, about 1.2 per cent. Adami and McCrae[4] found perforation twice in 85 autopsies on chronic pulmonary tuberculosis, or a frequency of 2.35 per cent. In my 475 autopsies there were 13 instances of intestinal perforation, or 2.7 per cent.

Fenwick in his statistics takes into consideration only those cases that showed what he termed a "complete perforation." By that he means the ulcer had perforated directly into the peritoneal cavity and caused either acute peritonitis or a local abscess. He terms partial perforation those cases which, due to the local peritonitis from the ulceration, have formed adhesions with some other knuckle of gut before the ulcer has perforated. These cases do not cause acute general peritonitis, as the ulcer perforates on to the peritoneal covering of the section of gut to which it is adherent, and there is no extravasation of fecal matter into the general peritoneal cavity. Sometimes these cases ulcerate through the adherent portion of gut and form a fistula between the two segments of the intestine. Von Rindfleisch[5] reports an interesting case in which "five tuberculous ulcers of the ileum had perforated, not, however, into the peritoneal sack, but into divisions of the bowel,

[1] Nothnagel's Encyclopedia of Practical Medicine.
[2] The Dyspepsia of Phthisis.
[3] Quoted from Fenwick.
[4] Proceedings of the Sixth International Congress on Tuberculosis, vol. i, part i, p. 330.
[5] Pathological Histology, New Sydenham Society's Transactions, p. 419.

which had previously become adherent opposite the seat of ulceration. This, of course, put a stop to all peristalsis, the products of digestion circulating without any order through numerous false passages in the abdominal cavity, inasmuch as the fistulous communications were in some cases wider than the caliber of the intestinal tube itself."

Following Fenwick's classification, of my 13 cases, 10 were complete perforations and 3 partial. Taking up, first, the complete perforations, 5 occurred in men and 5 in women, and the average age of the patients was thirty-two and one-half years. The small gut was the site of the perforation in 6 instances and the large one in 4. Of the 6 cases in the small gut, 5 are definitely stated to have occurred in the ileum, and in 1 case the notes do not specify whether the perforation was in the ileum or the jejunum. Two cases showed two complete perforations, and 1 case as many as four; in another the notes do not give the number, but state that "there were numerous perforations of typical tuberculous ulcerations." Acute peritonitis was present in 4 cases, and purulent peritonitis in 2.

Of the perforations occurring in the large gut, 3 were in the appendix and 1 in the head of the cecum. In one of the appendiceal cases the appendix had completely ulcerated off at the tip, and in another there was a perforation at the base of the viscus. The third case showed the appendix swollen near the tip and communicating with another mass to the left. Upon opening this mass purulent material was found and there was a perforation near the tip of the appendix.

Acute peritonitis was present in the perforation of the cecum and in the perforation at the base of the appendix. In the case where the tip of the appendix had completely ulcerated off there was purulent peritonitis. In the local abscess the peritoneum was normal.

The three partial perforations, those in which the perforation was walled off by adhesions, occurred in men, and the average age of the patients was forty years. The ileum was the seat of the disease in 2 instances and the transverse colon in 1. In the cases occurring in the ileum, one showed a single perforation and the other showed multiple perforations. The single perforation was 1.5 by 1.5 cm. in size, and in the multiple perforations one was 1 by 2 cm. In the perforation of the ileum the general peritoneum was normal; in the case with multiple perforations there was a general tuberculous peritonitis. The peritoneum, in the perforation of the transverse colon, showed only a localized peritonitis, the parietal layer of the peritoneum being apparently normal.

The clinical symptoms of perforations of the intestines in most conditions are usually distinctive and characteristic. There is first the sudden violent pain that occurs with the rupture of the bowel, said to be due to irritation of the nerves in the peritoneum.

The patient is in a condition of shock with pinched face, subnormal temperature, rapid running pulse, and often nausea and vomiting. At first the abdomen is rigid though it may be distended if gas has escaped into the free peritoneal cavity. Death may occur in a few hours, due to shock. If the patient survives the shock the symptoms of acute peritonitis develop. The temperature begins to rise, the pulse becomes more rapid, the abdomen, if not so before, becomes distended and painful. Nausea and usually intractable vomiting begin.

If such was always the picture in perforation of a tuberculous ulcer of the intestine the condition would not pass undiagnosticated so often. But it is a well-known fact that there can be advanced disease of the peritoneum in chronic tuberculosis without any marked symptoms or clinical signs.

Four of my cases of complete perforation had fairly typical symptoms and signs. Case No. 2360, a woman, aged thirty-three years, admitted to the wards on May 23, with no abdominal symptoms. On the thirtieth of the month she developed diarrhea. On June 13 she complained of marked pain in the abdomen. Abdomen was distended and quite rigid on the left side, and pressure in this area produced considerable pain. The temperature dropped to subnormal and the pulse went from 120 to 148. On June 14 the patient was in a state of collapse, with the abdomen greatly distended, tympanitic, hard, and painful. She had marked diarrhea. On June 15 her face was pinched, she was extremely weak, but had no pain, and the diarrhea had stopped. She died that evening. The autopsy showed a single perforation in the ileum and a purulent peritonitis. Case No. 2311, a man, aged twenty-four years, was admitted to the wards on April 23, complaining of diarrhea with cramps for three months. Abdomen was tense and painful and probably contained fluid. On April 30 he was seized with intense pain in the abdomen. The abdominal walls were hard and board-like. Temperature dropped from 101° F. to 95°, and the pulse went from 110 to 158. He died the next day, and the autopsy showed two perforations in the ileum and an acute peritonitis. Case No. 734, a woman, aged thirty-five years, was admitted to the wards with diarrhea. On February 16 her temperature became subnormal, her pulse much more rapid, and she lay in a stuporous half conscious condition. On February 20 her diarrhea stopped. A few days before her death her mind became clear. The autopsy on February 26 showed a perforated ulcer at the head of the cecum and an acute peritonitis. Case No. 4140, a woman, aged twenty-two years, admitted to the wards on May 14, with slight diarrhea, but no pain or tenderness in the abdomen and no rigidity. On May 21 she complained of pain in the abdomen; the next day the pain was very severe and accompanied by a slight fall of temperature but no change in the pulse rate, which was already

quite high. On May 29 she died, and the autopsy showed two perforated ulcers in the lower part of the ileum and an acute peritonitis.

The first two cases, particularly the first one, are typical case histories of perforation of the intestine, and with such data occurring in an advanced case of phthisis, a diagnosis of perforation of a tuberculous ulceration should be made. The last two are not so typical, but are suggestive enough to make one think of the possibility of perforation.

It is in the cases where the symptoms and signs are indefinite that autopsy findings are surprising. In 5 of my cases the symptoms were most indefinite. Two had absolutely no abdominal symptoms, 1 had pain in the abdomen but no other symptoms, 1 had pain, tenderness, and rigidity, with some slight change in temperature and pulse, and another showed only a drop in temperature. When it is remembered that all these signs and symptoms are found in a great number of cases which at autopsy only show ulceration of the intestine and perhaps some localized peritonitis, it is easy to realize how impossible it is to diagnosticate the condition in life.

The case of localized abscess had no diagnostic symptoms. There was diarrhea and some tenderness, but no mass was noted. Fenwick says that "a fecal abscess cannot be looked upon as a complication of chronic phthisis endowed with any symptoms more striking than those of chronic local peritonitis."

In the partial perforations the symptoms were no more than are found in a great number of chronic cases of phthisis. One had pain, tenderness, and the abdomen was tense and distended. Another complained of diarrhea and abdominal cramps, but had no tenderness and no rigidity. The third one had abdominal pain alone. I found in the analysis of the symptoms of the 462 cases who had no intestinal perforation that diarrhea was present in 49 per cent., tenderness in 22 per cent., pain in 20 per cent., and rigidity in 14 per cent. Hence, if all these symptoms occur in cases without perforation, how futile it is to try and diagnosticate a perforation from them alone.

Conclusions. 1. Perforation of the intestines in chronic pulmonary tuberculosis occurs in from 1 to 5 per cent. of cases.

2. It is possible to diagnosticate complete perforation in only a limited number of cases.

3. It is only possible to diagnosticate local abscess due to perforation when the mass can be felt.

4. It is never possible to diagnosticate with certainty a partial perforation.

PRENATAL AND INFANTILE TUBERCULAR PREDISPOSITIONS.

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All physicians are now familiar with what may be termed the technical prophylaxis of tuberculosis—how to deal with the tubercle bacillus and its bacterial congeners (which with it make up the mixed infections)—we know now thoroughly how to deal with the inhalation, ingestion, and inoculation types of infection in this disease. But there is a prophylaxis of tuberculosis predispositions at least as essential as that which is concerned with the specific cause; and this paper has to do with the prevention of such of these predispositions as may obtain up to the period which terminates infancy.

I am reminded of the Hibernianism of Oliver Wendell Holmes—that "a man should be careful in the selection of his ancestors." To fortify the organism with a view to enabling it to withstand infection, we must begin long before the birth of the individual concerned. In science, birth is but an incident in a succession of life processes; conception is but a transmutation of older cellular elements, such as are contained in the ovum and the sperm, into a new cellular compound. And it is after all with the quality and the virility of cells that we have primarily to deal. The practical deduction here is that those contemplating marriage who seek our advice, should be urged to proceed with the greatest circumspection and self-restraint, if they are conscious of any abnormal stigmata—any indications of degeneracy in themselves, either ancestral or acquired. Undoubtedly the possibility of parentage on the part of men and women who are unfit for this tremendous responsibility—the nearly related, couples of widely diverse ages, the neurotic, or pervert, or insane, the drug habitués, the syphilitic, the consumptive, and above all the alcoholic—the possibility of parentage among these should be precluded whenever this can possibly be done; generally speaking, all such subjects are likely to transmit to their offspring vitiated tissues, upon which the Koch bacillus and its bacterial allies may with unusual ease find implantation.

The principle of "natural selection" will, much more frequently than is assumed, act to prevent such marriages; this law of nature is infinitely more effective than any human legislation on the subject. However, when in these premises a physician is consulted, he should, as earnestly as may be, deprecate marriage; but emphatically should he countenance no marriage when tuberculosis

is active in either man or woman. Especially should no tuberculous woman be permitted to marry. In her case there is ever the possibility of death in childbirth, the probability—should that crisis be survived—of physical wreck and death by lingering stages subsequent to delivery. "Pregnancy is found to complicate, to precipitate, or to develop phthisis remarkably." And "when consumption is hanging about a girl, the distance between the marriage-bed and the grave is usually short with her; the husband if he does not become a widower soon after the birth of the first child may count upon a perpetually ailing wife." And, for the other side of the picture: "Many a young man has sacrified his chance of recovery on the altar of Hymen."

A consumptive should not marry a person in health, especially if the disease has existed a long time and is progressive; besides, a latent and comparatively innocuous lesion may through marital stresses develop an active and a fatal issue. But should one who has been consumptive, and who now does not evidence tuberculosis, marry? A patient who for two years has had no physical signs (except those of a healed lesion) and no other discoverable symptoms may be allowed to marry. Emphatically there should be no marriage while the disease is in progress; however, after there has been a relative recovery, when the symptoms have been in abeyance for two or three years, and a satisfactory general condition has been maintained, marriage need not be objected to (Cornet). If a man be financially fortified against the possibility of want or poverty, and if his wife makes no great or undue sexual demand upon him, he may be better off married than a bachelor—with all the unhappiness and discomfort contingent upon that unworthy and unfortunate state. On the other hand, a woman may be seriously harmed by marriage, with all its taxes upon the feminine organism. For wifehood, she should be strong and toned up beforehand, not only for her own sake but especially for that of her offspring. Conception must be advised against in consumptive women; they stand the puerperium badly. The disease often assumes its most acute form after childbirth, and then proves rapidly fatal. To save the maternal life interference may have to be counselled. Multiple births should be discouraged for such mothers.

Having thus dwelt upon the melancholy aspects of this question, its brighter side should receive due consideration. Although the observation generally holds good that tuberculous parents will have offspring with organisms prone to tuberculosis, there are many unquestionable cases, such as have been recorded by Flick, King, Cornet, and others, in which the offspring of consumptive parents have been found singularly immune to that disease. There are such marriages that have been blessed with perfectly strong and well-developed progeny. It would seem indeed, in such cases,

that the offspring is more immune to tuberculosis than infants not thus born. Possibly this is by reason of an acute exacerbation of tuberculosis in the mother, in which phase of the disease an immunizing antitoxin has been developed, and thus transmitted to the embryo in the maternal blood.

Though the marriages of consumptives are likely to be unfortunate, this does not always follow. A venerable gentleman once related to me how in his youth his mother had counselled him not to marry his beloved, who was consumptive. Nevertheless they did marry, and immediately after exchanged urban for country life. This was many years ago, when consumptives were put in superheated, malodorous, hermetically sealed rooms (so that no draught might assail them), and were made to swallow nauseating syrups until they died; before our profession was prescribing sunshine, fresh air, and good food in the treatment of tuberculosis. This courageous man went at once to the rural butcher and made arrangements for the best meats to be sent regularly to his house. Then he went to a vegetable farmer and asked him to name his price (that was no object; no matter what it was it would be paid) for the privilege he desired of going among those vegetables as often as he liked and of carrying off as much as he should wish to. And thus to others who had good nutriment to sell. And so this couple lived together, practising essentially the principles of therapy we now follow in tuberculosis; and the wife did not die of consumption, but achieved good health, and lived to bless that superb husband, through many years, to a fine old age.

When a consumptive has married, the pair should be counselled not to have intercourse in times of physical or psychic fatigue, or during such ill health as would intensify the original affection. When conception has occurred, we recall that during embryonic life the cells of the body become differentiated, and the organs are formed, increase in size, and begin to take on their several functions; that during this period the organism of the coming infant is most acutely sensitive to environmental impressions—such as variations in oxygen supply, warmth, and the constitution of the maternal blood. Before the birth, then, the mother should be safeguarded to the fullest possible extent, for the good of her offspring; she should, even more so than in ordinary pregnancies, be assured wholesome diet; sensible and hygienic clothing; should rest well at night, and for an hour after lunch; have frequent baths in tepid water, and the like familiar measures; especially should she be subjected to no unusual mental strain or excitement.

If, unfortunately, the child at birth exhibits stigmata, either functional or anatomical, we have to act without delay; and, of course, our therapy will here be a matter not of weeks or months, but of years. Here is the legitimate office of the family doctor; the specialist must be consulted from time to time, but the

family doctor, in his peculiarly intimate relationship, must have the medical bringing up of that child. Here he may have to deal with manifestations of the scrofulous temperament—the pallid skin and flabby flesh; tedious and subacute mucous membrane inflammations; enlargements of the lymph glands; unhealthy throats, bronchitis, gastrointestinal affections, sluggish metabolism. There may be strumous chest malformations; deficient ossification; stunted and weazened growth; breathing capacity below the average; defective circulatory development; perhaps an undersized heart and aorta, and anemia.

Rectification to the normal average may be impossible. Nevertheless, everything should be done to mitigate abnormal conditions as much as may be, not only for the sake of the child itself, but for the avoidance of baneful effects upon future generations. It is most encouraging to recall that functional aberrations from the normal, while more likely to be transmitted than anatomical stigmata, are, nevertheless, more amenable to treatment. Anatomical stigmata (if I understand the embryologists aright) are evolved out of functional stigmata. Although there may be no definite anatomical stigmata, a pernicious nutritive habit is often transmitted, which it is the business of the physician to detect and to cope with. Such patients, as intimated, will have to be kept under constant observation, not for weeks or months, but for years.

A weak and consumptive mother should not nurse her infant. There is little likelihood of her milk itself being infected (there is much more likelihood of the infant being infected by the mother's cough, as it lies upon the breast). But the milk of such a mother is not, in general, sufficiently nutritious; besides, lactation is a great drain upon her already depleted strength, and may precipitate a fatal termination, and that before the time when such breasts are naturally dry. Either a wet-nurse should be found or the infant should be bottle-fed. The latter is now the better way, in view of the profession's remarkable advances in infant feeding. In large cities, both public and private charities have become so beneficently active in this regard that the poorest people may have excellent milk, properly modified, at little cost, or, if need be, at no cost at all. Especially is it fortunate, I believe, that municipalities are now in general committed to pasteurization. While ingestion infection is perhaps infrequent among adults, I have for my part never made any doubt of the deplorable frequency in infants and children of latent tuberculosis by reason of the bovine tubercle bacillus in milk.

The separation of an infant from a tuberculous mother is a matter not easy of adjustment or decision. Certainly, there is little occasion if the mother be conscientious and properly instructed and if the infant be bottle-fed. The maternal impulses should receive much consideration. Such separation is often

impracticable among the poor. In many cases among the poor it were well if the mother would have her child taken care of for part of the day in a general nursery, such as the charitable provide in cities. Many poor people cannot be without their children; many are not willing to be; separation should not be, nor can it be, compelled. In any event, the infant's home should be made free of infection by and thorough and frequent purification and by disinfection occasionally. The floors should be particularly clean, and carpetless if possible, rugs (which may be frequently renovated) being substituted. The infants should be properly clothed and bathed. Dr. Abraham Jacobi has made notable observations on the hardening of the infant. Adenoids and hypertrophied tonsils should be removed, or at least treated. The child must not be starved for oxygen. Sleeping children should have plenty of air; sleeping garments of the grain-bag construction should be provided them. All respiratory and circulatory affections should receive unremitting attention. Convalescents from diphtheria, pertussis, measles, scarlet fever, and so forth, should be carefully nurtured, and, if possible, sent into rural districts. Headaches, purulent otitis medias, and abdominal symptoms should be promptly attended to, as also accidents and, very imperatively, injuries involving bones and joints. Most of these lesions in infants and young children are or become tuberculous. All young structures are less firm, less organized, and more vulnerable than those of the adult. The child should as early as possible be taught not to swallow its sputum or the excretions from its upper air passages; these are frequently bacillus-laden, and may engender intestinal tuberculosis.

THE LEUKOCYTIC PICTURE IN PULMONARY TUBERCULOSIS.[1]

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In order to determine whether in pulmonary tuberculosis any relationship exists between the different types of leukocytes and the extent and progress of the disease, we have made 182 differential

[1] Read before the Philadelphia County Medical Society, October 26, 1910.

blood counts on 50 tuberculous patients. The latter were under the care of one of us in the Home for Consumptives, Chestnut Hill, and in the Philadelphia Jewish Sanatorium for Consumptives, Eagles-ville, situated 500 and 600 feet, respectively, above sea level. The one who made most of the counts knew nothing about the condition or progress of the patients. The number of blood counts in the individual cases varied from one to nine. The blood was stained with eosin and hematoxylin.

We classify the white cells as polymorphonuclear neutrophiles, which are subdivided according to the number of nuclei they contain, lymphocytes, mononuclear cells, transitional cells, polymorphonuclear basophiles, and eosinophiles. Of the mononuclear basophilic cells, we designate as lymphocytes those in which the nucleus occupies more than half of the cell, and as mononuclears those in which the protoplasm equals or exceeds the nucleus in size. We regard such a classification as more rational and less liable to personal error than one in which the cells are differentiated by their size.

The patients are grouped in three stages, as incipient, moderately advanced, and far advanced, and as apparently cured, arrested, and improved cases, according to the schema of the National Association for the Study and Prevention of Tuberculosis, and, in addition, as stationary and advancing cases. They are also classified according to the extent of the disease in the lung, as recommended by Turban. Patients in the third, or far advanced, stage we further subdivide into those capable of working and those incapacitated, the latter being again subdivided into those that are toxic and those that are not.

The following tables give the average proportion of each type of cell we found in the different groups, and the number of cases and blood counts on which the averages are based:

	No. of cases.	No. of blood counts	Polymorphonuclears.	Lymphocytes	Mononuclears.	Transitionals.	Eosinophiles.	Arneth I and II.
All stages	50	182	66.0	30.0	1.5	1.0	1.5	44.5
Stage I (incipient)	13	46	62.5	33.5	2.0	0.5	1.5	44.5
Stage II (moderately advanced)	6	27	65.0	30.5	2.0	1.0	1.5	41.5
Stage III (far advanced)	31	109	68.0	28.5	1.5	1.0	1.0	44.5
Class I (Turban)	14	50	63.0	33.0	2.0	1.0	1.0	45.5
Class II (Turban)	9	36	65.5	30.0	2.0	1.0	1.5	45.0
Class III (Turban)	27	96	68.0	28.5	1.5	1.0	1.0	43.5
Apparently cured	5	24	61.0	35.0	2.0	0.5	1.5	43.0
Arrested	5	16	64.5	30.5	2.5	1.0	1.5	47.5
Improving	15	68	64.5	31.5	2.0	0.5	1.5	44.0
Stationary	9	30	69.0	28.5	1.0	0.5	1.0	32.0
Advancing	15	43	68.5	27.0	1.5	1.5	1.5	45.0

In the following table the patients in each stage have been grouped according to the progress of the disease:

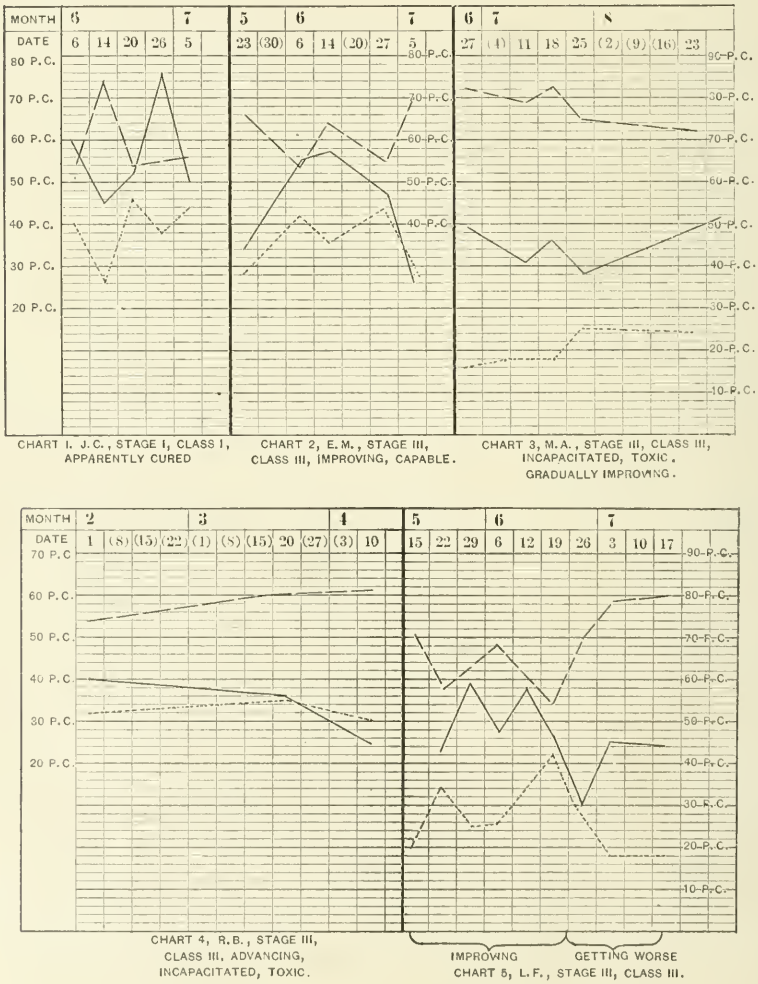
	No. of cases.	No. of blood counts.	Polymorphonuclears.	Lymphocytes.	Mononuclears.	Transitionals.	Eosinophiles.	Arneth I and II.
Stage I:								
Apparently cured	5	24	61.0	35 0	2.0	0.5	1.5	43.0
Arrested	3	6	66.5	29.0	2.5	1.0	1.0	52.0
Improving	5	16	62.0	34.5	1.5	1.0	1.0	42.0
Stage II:								
Arrested	2	10	61.5	33.0	2.0	1.5	2.0	40.5
Improving	2	13	66.5	28.0	3.0	0.5	2.0	49.0
Stationary	2	4	67.0	30 5	1.0	1.0	0.5	69.0
Stage III:								
Improving	8	39	65.8	30.4	2.0	0.4	1.4	46.7
Stationary	8	27	68.5	29.0	1.0	1.0	0.5	43.0
Advancing	15	43	68.5	27.0	1.5	1.5	1.5	45.5
Capable of working	9	37	64.5	32.0	2.0	0.5	1.0	43.0
Incapacitated	22	72	69.5	27.0	1.5	1.0	1.0	45.5
Non-toxic	8	35	68.0	29.0	1.0	1.0	1.0	46.5
Toxic	13	33	70.0	26.0	1.5	1.5	1.0	45.0

Polymorphonuclear Neutrophiles. A regular increase in the proportion of polymorphonuclear cells was observed with the advance in the stage of the disease and in the amount of lung involvement. This agrees with the results of Holmes,[2] Hultgen,[3] Swan,[4] and Craig.[5] We also found a smaller percentage of polynuclear cells in patients who were doing well, and a larger percentage in those doing poorly. It seems to us that the blood picture is influenced more by the progress of the disease and the patient's resistance than by the stage or extent of the process. The average pictures obtained in each stage we therefore attributed in large measure to the condition exhibited by the majority of the patients in that stage. That it is the condition of the patient that is responsible for the blood picture rather than the stage or the extent of the disease, is brought out particularly well in our minuter subdivisions of Group III.

Webb and Williams[6] found the smallest number of polynuclear cells in normal cases, the next highest in order being cured, improving, stationary, and advancing cases. The experiences of Pavillard,[7] d'Oelsnitz,[8] and Arloing and Gentry[9] were practically similar.

[2] New York Med. Rec., 1896, l, 325.
[3] Trans. Chicago Path. Soc., 1909, vii, 199.
[4] Jour. Amer. Med. Assoc., 1904, xlii, 697.
[5] Fourth Annual Report of Henry Phipps Institute, Philadelphia, 1908, p. 108.
[6] Trans. Nat. Assoc. for the Study and Prevention of Tuberculosis, Philadelphia, 1909, p. 231.
[7] Thèse de Paris, 1900.
[8] Ibid., 1903.
[9] Lyon Méd., 1910, cxiv, 966.

Since we read our paper, Wright and King,[10] Dominguez,[11] and Miller and Reed[12] have also reported practically similar results. Sondern[13] regards an increase in the relative number of polynuclear cells as a direct indication of the severity of the toxemia. Bezançon, de Jong and de Serbonnes[14] always observed a moderate transitory increase in the polynuclear cells just at the beginning of what they



The broken line indicates the percentage of polymorphonuclear cells, the continuous line the percentage of polymorphonuclear cells with one and two nuclei, and the dotted line the percentage of lymphocytes.

[10] Amer. Jour. Med. Sci., 1911, cxli, 852.
[11] Sanidad y Beneficencia, Havana. 1911, v, 449.
[12] Jour. Amer. Med. Assoc., 1911, lvii, 504.
[13] Boston Med. and Surg. Jour., 1905, cliii, 690.
[14] Arch. de Méd. expér. et d'anat. path., 1910, xxii, 17.

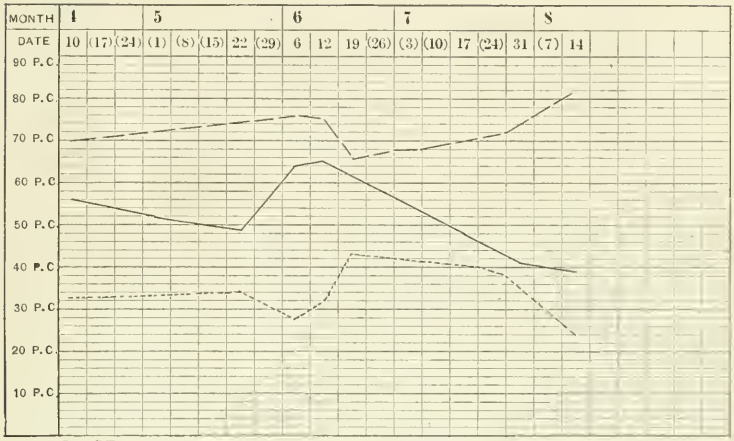


CHART 6. A.K., STAGE III, CLASS III, ADVANCING, INCAPACITATED. NON-TOXIC.

No counts were made on the dates in parentheses. The lines have the same significance as in the preceding charts.

term an evolutive progression or exacerbation, and a marked increase in galloping consumption and in grave forms of the disease.

Arneth's Classification of Neutrophiles. The neutrophilic cells were divided in accordance with the number of nuclei they contained, as first practised by Arneth.[15] In the tables are recorded the percentage of neutrophilic cells with one and two nuclei, which many take as an index, 45 to 55 per cent. of these cells being regarded as normal. The average index we obtained in each group was practically normal. While the average index showed little change, in most of our individual cases the proportion of cells in the first two classes of Arneth seemed to be increased as the patient improved, and in a number of cases to be diminished as the patient grew worse. In many instances the rise would be maintained only for several weeks. Of 27 improving patients, whose blood was examined more than once, an increase in cells with one and two nuclei was observed in 22, and a decrease in 4. Among advancing cases there was an increase in 3, a decrease in 4, and no change in 2. The blood charts of several cases are given, showing this change.

Our figures are opposed to those of all other workers. Arneth, Achard,[16] Arloing and Gentry, Bushnell and Treuholtz,[17] Dluski and Rospedzihowski,[18] Edson,[19] Klebs and Klebs,[20] Minor and

[15] Die Neutrophilen weissen Blut Korperchen bei infections Krankheiten, Gustav Fischer, Jena, 1904.

[16] Semaine Méd., xxix, 517.

[17] Med. Record, 1908, lxxiii, I, 470.

[18] Proc. of Sixth Internat. Cong. on Tuberculosis, Philadelphia, 1908, i, 1143; Beiträge zur Klinik der Tuberculose, Würtzberg, 1909, xiv, 259.

[19] Trans. Amer. Climat. Assoc., 1909, xxv, 52.

[20] Amer. Jour. Med. Sci., 1906, cxxxii, N. S., 538.

Ringer,[21] Webb and Williams,[22] von Borsdorff,[23] Wolff,[24] and Sabrazès[25] state that in favorable and improving cases there is a decrease, and in unfavorable cases an increase, in the number of neutrophilic cells with one and two nuclei, at the expense of those with three, four, and five nuclei, the increase being greater the more severe the case. This was also the experience of Miller and Reed.

Whether altitude has any effect on Arneth's index cannot be deduced from the articles quoted, as the authors fail to give the altitudes of the sanatoria where they were working. It might be mentioned in passing that Minor and Ringer count nuclei connected by a distinct isthmus as one nucleus; that all the cases quoted by Bushnell and Truholtz do not bear out their statements; that of Webb and Williams' figures, which give only the maximum and minimum, the latter does not agree at all closely with Arneth; and that the average normal index is 48.5, according to Minor and Ringer, and 65, according to Webb and Williams.

Lymphocytes. In our cases the average proportion of lymphocytes was less the more advanced the stage of the disease, the greater the amount of lung tissue involved, and the more unfavorable the condition of the patient. There is but one exception to this, arrested cases holding a position between improving and stationary caes. On subdividing Stages I and II, according to the patient's condition, more exceptions to this rule are observed, due possibly to the small number of cases in each subgroup. In the third stage, however, which numbers more cases, the regular diminution in the lymphocytes in the more advanced cases is beautifully shown.

Additional evidence that the blood picture represents the resistive power of the patient, rather than a certain stage of the disease, is furnished when the patients in the third stage are subdivided into those capable of working and those incapacitated.

In the individual patient the proportion of lymphocytes was seen to increase as the patient improved and to diminish as he grew worse. Of 40 patients who were examined more than once, changes in the proportion of lymphocytes occurred in 32; 27 patients improved while under observation, 17 of these showing an increase in the proportion of lymphocytes, 8 a decrease, and 2 no decided change. Among 9 patients that grew worse while under observation, the lymphocytes were increased in 1, diminished in 6, and unchanged in 2. Of 4 patients whose condition remained stationary while under observation, the lymphocytes were increased in 1 and diminished in 3.

[21] Trans. Amer. Climat. Assoc., 1909, xxv, 37; Amer. Jour. Med. Sci., 1911, cxli, 638.

[22] Personal communication to Minor and Ringer; Colorado Med., 1911, viii, 175.

[23] Folia hæmatol, i; Archiv., 1910, ix, 242.

[24] Die Kernzahl der Neutrophilen, Heidelberg, 1906, Carl Winter.

[25] Arch. d. mal. du cœur, 1910, iii, 484.

A decrease in the proportion of lymphocytes as the disease becomes more advanced was also observed by Craig, Hultgen, and Strauss and Rohnstein.[26] Miller and Reed's observations were also similar. Cabot[27] states that an increase in lymphocytes is not peculiar to tuberculosis, but occurs in a variety of debilitated conditions. Holmes says that as the tuberculous condition becomes less marked and convalescence increases, the percentage of lymphocytes increases. Webb and Williams found the proportion of lymphocytes highest in normal persons, and then gradually lower in cured, improving, stationary, and advancing cases, respectively. Arloing and Gentry noted that an increase in mononuclear cells occurred in favorable forms of the disease. According to Bezançon, de Jong and de Serbonnes, in each progression the first stage of polynuclear increase is succeeded by a second stage of increased mononuclear cells. Richard's[28] forms of resistance to tuberculosis of attenuated virulence they found characterized by a sufficiently pronounced increase in lymphocytes. They state that the establishment of an increased proportion of mononuclears indicates in a general way a tendency to improvement. (This last statement has been confirmed by Wright and King and by Miller and Reed. Dominguez states that tuberculosis of medium virulence is distinguished by a marked lymphocytosis without evident mononucleosis. He also finds a lymphocytosis in laryngopulmonary tuberculosis and in bronchopneumonic tuberculosis.)

Mononuclears and Transitional Cells. The mononuclear and transitional cells in our cases show practically no changes with the advance of the disease, as indicated by the process in the lung, or by the patient's condition. (This was also the experience of Wright and King.) Craig, who obtained a much larger proportion of transitional cells than we did, found the smallest percentage in cases belonging to the second stage, and the largest in those belonging to the third stage of the disease.

Eosinophiles. The percentage of eosinophiles in our cases was unaffected by the stage or extent of the disease or by the condition of the patient. (Wright and King are in agreement with us upon this point.) Hultgen, Webb and Williams, Swan, Swan and Karsner,[29] d'Oelsnitz, and Bezançon, de Jong and de Serbonnes, however, found that the proportion of eosinophiles diminishes as the patients grow worse and increases as they improve. This latter fact was also observed by Arloing and Gentry and Wile.[30] (Dominguez and Miller and Reed also observed this latter fact.)

According to Bezançon, de Jong and de Serbonnes, at the

[26] Die Blutzusammensetzung bei den verschiedenen Anamieen, Berlin, 1901, Hirschwald, p. 74

[27] Clinical Examination of the Blood, fifth edition, New York, 1904, Wm. Wood & Co., p. 296.

[28] Quoted by Bezançon, de Jong, de Serbonnes, Province Médicale, 2 Mai, 1908.

[29] New York Med. Jour., 1907, lxxxv, 539.

[30] New York State Jour. Med., 1910, x, 205.

height of the second stage of the progression the number of eosinophiles commences to rise, this terminal eosinophilia seeming to these authors the most fundamental characteristic of the evolutive tuberculous progression, being maintained long after the clinical symptoms are improved. In a careful study of many cases, some over long periods of time, we were unable to confirm these observations.

No one has as yet given the eosinophilic picture obtained in tuberculosis according to Arneth's[31] method of subdividing the eosinophile cells into four classes, based upon the number of nuclei they contain.

Conclusions. 1. Improvement in pulmonary tuberculosis is associated with an increase in the proportion of lymphocytes in the blood at the expense of the polymorphonuclear cells. As the patients grow worse the proportion of polynuclear cells increases at the expense of the lymphocytes. None of the other types of white cells are affected by either condition. As a consequence, the percentage of lymphocytes will usually be less and the percentage of polynuclears will be greater, the more advanced the disease and the greater the amount of lung tissue involved.

2. As a patient begins to improve there is usually an increase in the proportion of polynuclear cells containing one and two nuclei, the increase often being maintained for several weeks, but not indefinitely.

3. Mononuclear, transitional, and eosinophile cells are unaffected by the stage, extent, or progress of the disease.

4. The leukocytic picture in pulmonary tuberculosis corresponds with the patient's resistance to the disease rather than with the extent of the lesion.

5. By means of the leukocytic picture it is often possible to determine the resistive power of a tuberculous patient and to form a fairly accurate estimate of the chances for recovery.

THE NORMAL DIFFERENTIAL LEUKOCYTE COUNT.

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When one endeavors to interpret the blood picture of a disease, it is obvious that he must know the normal differential leukocyte count. I have always accepted the Ehrlich percentages as commonly taught, but recently, in checking the results of a study of

[31] Deut. Arch. f. klin. Med., 1910, xcix, 19.

the blood in Hodgkin's disease, I was led to make a few differential counts on people who were, to all appearances, normal and in good health. These counts were at variance in some respects with the ordinarily accepted leukocyte picture, and in consequence I extended my series to counts on 25 persons, in order to be certain that in my first few counts I was not dealing with individuals whose blood happened to have the same peculiarities. The results of these 25 counts are still at variance with the text-book picture, and while the series is perhaps not extensive enough to overthrow that picture, yet the results as set down may be accepted as an accurate representation of the blood of individuals for the age indicated.

In glancing over the counts given in the various text-books on clinical microscopy and clinical medicine, one finds that there is considerable variation in them, and further that there is an entire absence of data as to the number or age of the individuals upon whom the counts are based. The following percentages have been gleaned from the text-books readily at hand, the leukocytes being divided into five or six classes, according to the working classification of Ehrlich: Polymorphonuclear neutrophiles (N.); eosinophiles (E); basophiles (Mastzellen) (B); small mononuclears (lymphocytes) (S. M.); large mononuclears (L. M.), usually including transitionals (Tr.).

Author.	N.	E.	B.	S. M.	L. M.	Tr.
Ehrlich and Lazarus (in Nothnagel)	70–72	2–4	0.5	22–25	1	2–4
Simon	60–70	1–4	0.2–1.0	20–30	1-6	
Cabot (in Osler)	60–70	0.5–3 or 4	0.1–0.5	20–40 of which	1–10	
Da Costa	60–75	0.5–5	0.5	20–30	4–8	
Stengel	65–70	3 or less	...	25	3–6	
Rotch	60–75	1–2	...	24–30	3–6	
Drysdale (in Allbutt)	66	1–3	0.5	25–26	2–4	
Krehl	70	1–4	0.5–2	25–28 of which	2–4	
Taylor	55–80	$\frac{1}{2}$–8	rarely seen	10–40	1–8	
Coles	70–75	...	...	15–20	6–8	
Von Limbeck	70–80	0.67–11				

Both Emerson and Sahli follow the figures of Ehrlich and Lazarus, accepting the rather narrow limits of variation in the neutrophile and lymphocyte percentages.

The counts presented below were made upon medical students and laboratory assistants, 23 of whom were men, and 2 women. With one exception they were in the first half of the third decade of life. The one exception was just above the age of thirty.

They were all in daily attendance upon university work, all apparently in health, and none conscious of any illness. Several of them were athletes in training. While the majority of the counts were made in the spring months, the rest were sufficiently scattered throughout the year to seem to indicate that season was not a factor. As a rule, though not invariably, the counts were made just before the noon hour

The blood smears have been stained with Wright's stain, and upon the basis of this stain I have divided the leukocytes into seven

classes, following the Ehrlich classification, with the exception that I have divided the lymphocyte group into large and small types. While the division of the so-called non-granular cells (on an Ehrlich stain basis) into four groups is somewhat arbitrary, and while one is sometimes in doubt just where to place certain individual cells, yet four distinct types of cells can be made out. These may be briefly described as follows:

1. *Small Lymphocyte.* A cell with deeply staining nucleus which scarcely exceeds a red blood cell in diameter, and with a scant rim of basophilic protoplasm.

2. *Large Lymphocyte.* A cell usually almost the size of a neutrophilic leukocyte, with nucleus larger than that of the preceding class, and with protoplasm more abundant, less basophilic as a rule, and containing numerous coarse almost rod-like metachromatic granules.

3. *Large Mononuclear.* A cell larger than a neutrophilic leukocyte, with a large round or oval nucleus and considerable protoplasm staining a fairly deep blue and containing at times a few fine metachromatic granules.

4. *Transitionals.* The largest cells of the group, with nuclei of a variety of shapes, from simply indented forms to lobed, mulberry-shaped or even ring-shaped nuclei, and with abundant, clear, light-blue protoplasm thickly dotted with fine metachromatic granules which do not stain with Ehrlich's triple stain.

Upon this basis the following differential counts have been made, and they have been arranged according to the percentage of neutrophiles:

No.	Total count.	N.	E.	B.	S. L.	L. L.	L. M.	Tr.
1	9,000	68.6	2.2	0.2	14.6	5.2	2.0	7.2
2	7,600	64.4	3.4	0.0	15.4	8.6	1.4	6.8
3	6,800	62.6	0.8	0.8	18.6	9.0	1.8	6.4
4	12,000[1]	61.8	0.8	0.4	21.2	8.8	0.6	6.4
5	7,000	61.6	1.8	1.0	21.4	6.8	0.6	6.8
6	6,700	60.6	5.6	0.6	19.4	4.6	1.6	7.6
7	12,200[1]	58.8	3.8	0.6	28.0	7.2	0.8	8.8
8	8,800	58.2	4.0	1.2	21.0	8.6	0.6	6.4
9	6,700	57.2	2.4	0.0	21.2	7.6	1.8	9.8
10	8,000	57.2	2.0	0.6	24.0	6.4	1.0	8.8
11	7,000	56.8	3.6	0.4	17.8	11.4	2.4	7.6
12	6,000	56.8	1.8	1.8	20.2	10.8	2.0	6.6
13	6,800	55.2	3.6	0.8	20.4	10.0	1.2	8.8
14	9,600	55.2	3.0	1.0	34.0	3.2	0.4	3.2
15	7,000	55.0	2.2	0.6	28.0	7.2	0.8	6.2
16	6,300	53.8	1.0	0.6	25.2	11.0	1.0	7.4
17	7,000	53.0	1.6	1.2	27.4	5.6	1.2	10.0
18	6,300	52.2	0.8	0.6	20.2	16.0	3.4	6.8
19	5,700	51.6	2.4	0.4	33.2	3.8	1.0	7.6
20	8,500	51.0	2.6	1.6	20.6	16.0	2.2	6.0
21	7,500	50.8	6.8	1.4	19.4	11.0	2.8	7.8
22	5,900	45.6	4.2	1.0	35.2	4.8	0.8	8.4
23	7,000	42.8	3.2	1.2	25.0	13.2	3.6	11.0
24	8,900	38.0	6.2	1.2	27.6	17.8	3.0	6.2
25	5,000	37.4	9.6	0.6	24.8	16.2	3.8	7.6

[1] Verified at a subsequent date.

To summarize the counts briefly, one finds that the average of the total counts is 7,580, while 60 per cent. of the cases lie between 6000 and 8000, with a minimum of 5000 and a maximum of 12,000. Of the neutrophiles, 60 per cent. of the counts lie between 50 and 60 per cent., with the remaining 40 per cent. almost equally divided between those above 60 per cent. and those below 50 per cent. The average of the counts is 54.6 per cent. Further, 60 per cent. of the small mononuclears lie between 30 and 40 per cent., with 30 per cent. of the counts below 30 per cent. and but 10 per cent. above 40 per cent. The average is 33.1 per cent. The eosinophiles range from 0.8 to 9.6 per cent., with an average of 3.2 per cent., with 25 per cent. of the counts below 2 per cent., 25 per cent. between 2 and 3 per cent., 25 per cent. between 3 and 4 per cent., and the other quarter above 4 per cent. Basophiles range from "none seen in counting 500 cells" to 1.8 per cent.; the average being 0.8 per cent., and 40 per cent. of counts showing more than 1 per cent. The large mononuclears vary from 0.4 to 3.6 per cent., with an average of 1.6 per cent. The transitionals are about the most constant in percentage, 66 per cent. of the counts lying between 6 and 8 per cent., with but one count below 6 per cent., and but three above 9 per cent., the average being 7.4 per cent.

From this summary we may construct our probable limits for the percentages and our average count as follows:

	Total	N.	E.	B.	S. L. L. L.	L. M.	Tr.
		%	%	%	%	%	%
Probable limits	6000–8000	50–60	0.8–4.0	0.4–1.8	30–40	0.6–2.0	6–8
Average . .	7500	54.6	3.2	0.8	33.1	1.6	7.4

The points of difference between these counts and those cited earlier from the text-books are almost too obvious to mention. Briefly, however, no neutrophile count of the series is as high as the Ehrlich minimum, and 80 per cent. of the counts are lower than the minimum accepted by the majority of authors. On the other hand, the lymphocytes are above the maximum of the majority of the text-book counts, and the transitionals also are on the upper margin of the accepted normal. The other elements do not vary much from the usual figures.

It has puzzled me to explain these differences. While there are several possible explanations, the most probable seemed to be that the use of the Wright stain instead of the Ehrlich triple stain was largely responsible. In anything except a perfect Ehrlich stain the cells of the non-granular group are often so pale as to be easily overlooked, while with the methylene-blue-eosine stains both granular and non-granular cells are equally prominent. Comparative counts in my hands, however, showed no such difference, possibly because my attention was focussed particularly upon the mononuclear cells in the Ehrlich count. Another possibility is that

the lymphoid activity of adolescence may persist well into the third decade, so that one cannot expect the adult leukocytic formula until a later age. A few counts upon persons in the fourth decade not included in the list above do not bear out this assumption. It seems possible that the climate of Wisconsin in favoring chronic catarrhal conditions of the respiratory tract might be a factor. One might then expect a seasonal variation in the count, which was not found. Whatever may be the explanation, I am convinced of the accuracy of these counts for the age and the locality in which they were made, and feel that they must be taken into account in interpreting the blood picture of diseases common in the third decade.

STUDIES OF THE BLOOD IN DISEASE COMMONLY CALLED NERVOUS DISEASE.[1]

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AND

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There are few diseases of the nervous system that flow directly out of disorders of the blood. It is not the purpose of this communication to discuss such disorders. There are certain symptoms popularly called "nervous" which are dependent upon hemic states, and there are diseases of the viscera and of the blood that masquerade as affections of the nervous system. Such cases come to the neurologist in much greater number than the internist can readily believe. One of the objects of this paper is to emphasize the role that hematology plays in the pathogenesis of certain neurotic conditions. Before the establishment of the Neurological Institute we were not in a position to estimate either the frequency of occurrence of such disorders of the blood, or the diagnostic value that might be attached to them. We have been made aware that blood changes need not necessarily be pronounced in order to constitute a deviation from the normal. The trained eye readily sees changes in the various components of the blood, primary or secondary, which easily escape the eye that is not daily made familiar with slight deviations from the normal. Naturally we do not contend that there is a hematology for nervous diseases alone. We wish to maintain that the study of the blood in cases that present themselves for interpretation to the neurologist is

[1] Read before the Association of American Physicians, May 10, 1911.

one of the most fruitful fields for investigation. We are already in possession of a distinctive hematological picture in cases of paralysis dependent upon lead poisoning (lead neuritis, lead myositis), and plumbism may be diagnosticated as readily from examination of the blood as can malaria.

We are still far from a satisfactory understanding of the pathogenesis of the degenerations of the spinal cord and brain that flow apparently from certain anemias, and one of the problems of hematology is to determine the specificity of the anemias that produce such degenerations.

We propose to cite briefly a few cases which came to the Neurological Institute for interpretation and point out the importance that the study of blood conditions had in leading us to the correct diagnosis.

PROFOUND EOSINOPHILIA IN A CASE OF PITUITARY AND MEDIASTINAL TUMOR.

Case I.—A Jewess, aged thirty years, came September 12, 1910, complaining of pain in the right arm and in the back. This pain was of a sharp, shooting character, worse at night and rather paroxysmal in display; although she had some pain all the time, it was far worse at one time than it was at another. In addition to this, she complained of frontal headaches, which had been in existence for three weeks, of amenorrhea of six years' duration, and of loss of sight of the right eye. Her personal history could scarcely be construed to have any bearing upon her illness, which began three weeks before she presented herself at the hospital. It may be of interest, however, to know that she married at twenty-three, and soon after her menstruation, which had been previously regular, ceased. She had never been pregnant. She weighed 120 pounds when she married, and each succeeding year she gained about 10 pounds. The illness for which she sought relief began August 20, 1910, three weeks before she came to the hospital. The initial symptom was pain in the chest on the right side, then shortness of breath, which increased in intensity from day to day. She saw several physicians, but secured no relief. She had forgotten she had an attack of diplopia eighteen months before. It was not until August 25, 1910, she said, that her eyes began to bother her; objects were then blurred when she read or sewed; wearing of glasses produced no change; later she began to see double. Careful inquiry showed that in June, 1910, she had remarked that she could not see with the right eye. She was advised to consult a neurologist, who told the patient's husband that her brain was affected. She says, however, that until August 20 she was in the best of health, only experiencing some difficulty in breathing while ascending stairs.

At this time she was returning from Brooklyn, and at the Brooklyn Bridge was seized with a sick, dizzy, faint feeling. The neurologist who had diagnosticated the brain condition, advised cold compresses to the chest. During the next few days she began to feel feverish and to have chills and pains in the chest and back. It was then said she had pleurisy. She grew rapidly worse, very weak and nervous, restless and sleepless. The condition of restlessness and sleeplessness was ascribed to the ovarian extract which had been prescribed for her. About this time it was noticed that her face was puffed and swollen, and that she had considerable dyspnea. On September 14, 1910, when she entered the Neurological Institute, the following notes were made:

The patient in a semirecumbent position has labored breathing, at times gasping for breath. The face, which is puffed and slightly cyanosed, has an anxious expression. The facial lines are obliterated; the tongue coated.

Thorax: Chest, barrel-shaped, expansion on right side diminished; respirations, 36 per minute. Increased vocal fremitus over entire right lung. Complete dulness over right lung anteriorly. Posteriorly flat percussion note below the sixth rib. Bronchial breathing over entire right lung anteriorly. Absence of respiratory sounds posteriorly below the sixth rib; above that bronchovesicular breathing is elicited. A few small moist rales are heard at the end of respiration. Percussion note normal over left side of chest. Compensatory breathing over left lung.

Heart: Negative, save for an accentuation of the second pulmonic sound. Pulse, regular; equal on the two sides; 138 to the minute.

Abdomen: Negative, except for tenderness in the gall-bladder region.

Gynecological examination: Small infantile, movable uterus, with a long narrow cervix.

Ophthalmological examination: The right eye, which diverges slightly, has only bare perception of light. The left eye has vision of $\frac{20}{50}$. There is a left temporal hemianopsia for large test objects. The right optic disk is white, sharply outlined, and the vessels are of normal caliber. The left optic disk shows pallor of the left temporal half.

Examination of the cutaneous sensibility shows an area of hyperalgesia over the chest and the back. All the tendon-jerks were normal, but the abdominal reflexes could not be elicited.

The Wassermann reaction of the serum was negative.

Blood examination: Red cells, 4,848,000; white cells, 11,400. Differential count: Neutrophiles, 40 per cent.; large lymphocytes, 3 per cent.; small lymphocytes, 21 per cent.; eosinophiles, 31 per cent.; large mononuclears, 1 per cent.; transitionals, 4 per cent.

No degenerations in the red or in the white cells.

The eosinophilia was most striking, and the cause for it was diligently sought. The intestines gave no clue to its dependency. The only condition to account for it was the mediastinal and cerebral abnormality. The aspirated material from the chest, a sanguinopurulent, thick fluid, when examined microscopically showed many cells in a state of fatty degeneration. The bulk of the aspirated material consisted of large cells, not conforming to the usual findings in inflammatory exudates. The cells presented a large body almost entirely occupied by an intensely staining nucleus.

A tentative diagnosis of sarcoma of the pleura and of the mediastinum was made, and the patient was submitted to *x*-ray examination, with the following results: Two exposures made with the plate behind show the ribs, spines, and structure around the shoulder very distinctly. There is such a large accumulation of fluid in the pleural cavity that it is impossible to get any detail in the lung on the right side. The heart is slightly displaced to the left, and even the left lung is very much compressed.

From a study of the plates, viewed in a satisfactory light, one readily detected a mediastinal growth about five inches in diameter, the upper end of which was near the sternal notch. The clear-cut, defined edges indicated that this was a mediastinal tumor, but it could not be distinguished positively from an aneurysm.

The clinical interpretation was then, as it is now, that we were dealing with a malignant growth originally of the pituitary body, with metastasis in the thorax. That the former had been in existence many years was indicated (1) by the amenorrhea of many years' duration; (2) by the progressive increase of weight; (3) by the attack of diplopia which occurred eighteen months previous to the sudden monocular blindness; (4) by the blindness (hemianopsia); and (5) by the ophthalmoscopic evidence of pressure upon the optic chiasm.

The patient left the Neurological Institute soon after the diagnosis was made, and died, we are informed, about three weeks later.

The clinical features of the case do not call for special comment. The remarkable phenomenon was the eosinophilia. Although eosinophilia is an easily detectable state of the blood, very little is known of its significance, and still less of its pathogenesis. Ehrlich gives 4 per cent. as the normal upper limit, and 0.5 per cent. as the normal lower limit. There are cases recorded in which no eosinophiles were found in the blood, and cases in which 90 per cent. of the white cells were eosinophiles. In certain of the exanthemata, such as scarlet fever and rubeola, an eosinophilia always exists. In the former as high a count as 23 per cent. was found by Reckzeh.[2] In rubeola the eosinophilia, which appears, as a rule, during

[2] Deutsch. Archiv f. klin. Med., 1903.

desquamation, may reach 8 per cent. In pertussis, as the spasms begin to get less severe and rarer the eosinophiles increase in numbers, and may reach 15 per cent. The well-known eosinophilia in asthma may at times show as many as 33 per cent., and we have seen in one instance as many as 38 per cent. of these cells, which were diminished materially while the patient was being given adrenalin. It is well known that increase in the oxyphil cells is to be found most unvaryingly in helminthiasis. In the cestodic invasions, such as the Tænia solium, saginata, and nana, as a rule, no higher than 10 per cent. is obtainable. The anemia due to the Bothriocephalus latus is more destructive. The nematodes, such as the Ascaria lumbricoides, rarely cause more than 9 per cent.; Oxyuris vermicularis, 14 per cent.; Anchylostomum duodenale, 53 per cent.; Trichocephalus dispar and Anguilula stercoralis, about 13 per cent. The Trichina spiralis is capable of producing the highest known increase in the eosinophiles, and, according to Thayer and Brown,[3] as many as 68 per cent. have been found. In Bilharzia hæmatobium as many as 20 per cent. have been reported.[4] The highest reported in Filaria sanguinis hominis by the above author was 17 per cent.

Genuine uncomplicated rheumatic polyarthritis always shows an eosinophilia, which may reach as high as 11 per cent. In chorea one usually finds an eosinophilia of from 5 to 20 per cent. This is interesting, as the rheumatic joint affections also are accompanied by eosinophilia.

Although pernicious anemia does not, as a rule, show an increase in the eosinophiles, as many as 12 per cent. were found by Bloch and Hirschfeld.[5] My observations showed as many as 10 per cent. and as few as 0.2 per cent.

In leukemias one may find many eosinophiles or none, according to the stage of the disease and the rapidity with which it has developed. In marked tetany about 7 per cent. may be found. In carcinoma or sarcoma up to 8 per cent. have been reported. Gonorrhea in certain cases may show as many as 15 per cent.

The present status of hematology does not permit us to draw prognostic conclusions in gonorrhea from the study of the eosinophiles. A considerable number of the dermatoses are accompanied by eosinophilia; in pemphigus, as high as 33 per cent.; in dermatitis herpetiformis, as many as 27 per cent.; in prurigo, 11 per cent.; impetigo contagiosa, 8.2 per cent.; psoriasis, 17 per cent.; urticaria, as many as 60 per cent.; mycosis fungoides, 37 per cent.; lupus, 12 per cent.; lepra, 28 per cent.

The interesting feature in our case of eosinophilia was the large number of these cells, which, however, does not help in any way

[3] Lancet, September 25, 1897.
[4] Coles, Brit. Med. Jour., May 10, 1902.
[5] Berlin. klin. Woch., 1901, No. 40.

to exclude a nervous condition, nor does it help in localizing the affection. It may be cited as an example of marked eosinophilia in the course of a malignant tumor.

THE HEMATOLOGY OF SATURNISM.

The blood picture in certain cases of lead poisoning is very characteristic. Indeed, it may be considered nearly pathognomonic. As an illustration of this, the following case is cited:

Case II.—A man, aged forty-five years, who had worked as a lead smelter for twelve years, applied for admission to the Neurological Institute March 10, 1910. His complaint was of occasional cramps in the abdomen, which had existed for eighteen months or more, of inability to extend the fingers and hands (double wrist-drop), and of loss of strength in the entire upper extremities. The wrist-drop had developed on the right side in January, 1909, on the left in May, 1909, and the inability to use the upper extremities in February, 1910. The mode of development of his symptoms was indicative of the insidous way in which lead attacks and overcomes the peripheral motor neuron. Examination showed the typical picture of lead neuromyositis. The urinary examination revealed the presence of lead, and examination of the blood showed extensive and marked granular degeneration. The blood picture improved markedly after a course of judicious therapy, and kept pace with the somatic improvement of the patient.

The degenerative changes in the red cells, due to lead poisoning, are quite different from those due to other pathological states. The polychromatophilia is rare in lead changes. The granules in the red cells are also different from the granules found in secondary anemias. They are coarser, and the cells bearing them retain their original color or are slightly paler, whereas in similar degeneration of other blood diseases there is apt to be in the cell afflicted a more or less definite polychromatophilia.

The specific granular degeneration encountered in this case is the only neurohematological affection accepted. This change is not to be regarded in the light of a secondary anemia, but as a specific alteration due to the noxious influences of lead. It becomes quite evident that such is the case when lead eliminative therapy restores the blood morphology to its normal appearance. The modus operandi in the production of these granules is still in debate. Some claim that it is not a degeneration at all, but that the presence of the granules is an expression of protective forces of the body. This conception does not seem to us to carry sufficient corroborative evidence. We believe the granules to be a degenerative change rather than a hemoconvalescent phenomenon. It is a well-known fact that when blood analyses are made ante mortem in patients

who showed among other things granules in the erythrocytes, the number of such cells is very much increased as compared with smears taken during the incipiency of the disorder. When the patient recovers from his illness, the previously found granulations in the reds disappear, and this disappearance keeps pace with the improvement. A positive and negative phase has not been established in the appearance and disappearance of the granulations, and a convalescent significance can, therefore, not be applied to them.

SOME PHASES OF HYPOTHYROIDISM.

CASES III AND IV.—Two cases of nervous disease that do not admit of ready classification, in so far as they do not fit into any definite clinical picture, were those of brothers eleven and seven years old respectively. From a nosological standpoint they are perhaps best classified as dystrophies. The elder child's chief symptom is inability to talk distinctly. Words are not clearly enunciated, and he stops while articulating words and making sentences as if he were out of breath or tired. His hands tremble, he fatigues easily, he eats a great deal, and he never perspires. He goes to school, and he appears to be of average intelligence. He was late in beginning to walk, but he talked at the usual time. On examination the gait was somewhat of a waddling character, the spine showed a distinct scoliosis, the tendon-jerks were absent, and the boy was fat. The cutaneous reflexes were all elicitable. When he arose from a lying posture, it was not in a manner characteristic of the muscular dystrophies. The thyroid gland could not be palpated. Aside from these findings, the physical and mental examination was negative.

Examination of the blood showed: Hemoglobin, 73 per cent.; erythrocytes, 4,362,000; leukocytes, 9600. Differential count: Neutrophiles, 31 per cent.; eosinophiles, 13 per cent.; basophiles, 1 per cent.; large lymphocytes, 7 per cent.; small lymphocytes, 45 per cent.; transitional cells, 7 per cent.

The clinical picture of the brother was somewhat different. He was interpreted as an example of cortical focal encephalitis, occurring in a child possessed of some dystrophic condition of a family type.

This patient, aged seven years, was well up to his second year, when he had an attack of measles, during which he suddenly lost the power of speech, though he was still able to cry. It is said there was no paralysis of the face or of the extremities. Two and one-half years later, when he was above four years old, he began to talk again. At this time it was remarked that the right extremities were weaker than the left. He did not develop mentally as normal children do. His complaint when he was brought to the outpatient department of the Neurological Institute was weakness of

the right extremities, defective speech, mental retardation, and night terrors. Examination showed partial right hemiplegia; deviation of the tongue to the left; knee-jerk and ankle-jerk present on the right side, but absent on the left; Babinski toe phenomenon absent; all the superficial reflexes were present.

The Wassermann test was negative in both cases.

The blood analysis showed: Hemoglobin, 76 per cent.; erythrocytes, 4,680,000; leukocytes, 10,400. Differential count: Neutrophiles, 57 per cent.; eosinophiles, 4 per cent.; large lymphocytes, 7 per cent.; small lymphocytes, 31 per cent.; transitionals, 1 per cent. No abnormalities in the corpuscles.

Although the subject of blood changes due to various hyperglandular and hypoglandular functions is by no means firmly established, there is a tendency, as had been pointed out by Pineus and recently by Kocher, for the blood to respond in a more or less specific manner to disturbed functions of the ductless glands. The gland that receives the most attention is the thyroid. The nervous manifestations which disorder of the function of this gland is capable of producing are varied, but yet not fully recognized, therefore volumes are written on the subject. The hypofunctionating gland not only expresses itself in obesity, cretinism, and myxedema, but there are many other changes, somatic or psychic, that are the result of such malfunction. *Blood that shows a mild leukocytosis and a relative lymphocytosis with eosinophilia ranging from 3 per cent. up should be regarded as highly suggestive of a hypothyroid state.* The blood changes in the above two children presenting such a change, it was decided to class them among the hypothyroid clinical expressions, and thyroid extract was consequently prescribed.

The marked improvement that followed the administration of this substance is the chief reason for presenting the salient features in these two cases.

In these two cases of hypothyroidism there were no other changes save the relative lymphocytosis with eosinophiles mentioned. The difference between the two bloods in only conjectural. To what extent one child showed more of a hypofunctionating clinical picture than the other is not ascertainable in the light of our present knowledge of these conditions.

AN EXAMPLE OF PROMYELOCYTIC LEUKEMIA.

One of the most remarkable examples of blood disease masquerading as nervous disease, a case of acute leukemia resulting in acute transverse myelitis, is the following:

CASE V.—A young Russian Jew, aged twenty-nine years, was admitted January 23, 1911. His complaint was inability to stand or walk, inability to void urine or feces, pain in the middle of the

back. This pain was not severe, but at times subject to exacerbations. A sensation as if the legs and feet were asleep, and occasionally as if the legs were being squeezed. These symptoms came on abruptly ten days before coming to the hospital. During the first week of this time he was able to get about, so that in reality it was not until four days before coming to the hospital that he became paraplegic.

His history was uninteresting, save in one particular, and that was that he recalled on close questioning that seven weeks before the beginning of his ailment, he had what he called sticking pains in the left side of the abdomen in the region of the stomach. These pains continued more or less for three weeks. They were not severe, but nevertheless he consulted a physician, who prescribed for him, and soon after that the pains subsided. He denied syphilitic infection, and aside from having had his legs frozen when a boy of twelve years, he did not recall ever having been ill. He had served as a soldier in the Russian Army for three years (when he was from twenty-one to twenty-four years old), and after that he came to this country and began work as a picture-frame gilder. This occupation necessitated the use of amyl and methyl alcohol.

The first subjective symptoms of the illness which he had when he came to the hospital was a sharp, cutting, shooting pain in the small of the back and in the left side. Two or three days later his legs began to tingle and to feel as if they were asleep. Almost immediately he began to complain of weakness of the legs, and this continued to increase until at the end of the sixth day he was unable to stand or walk. From this time onward he was unable to void urine, and he had to be catheterized. By the time he was brought to the hospital he had a weak, ineffectual, hacking cough and constant dyspnea.

Examination showed that both lower extremities were flaccid and totally paralyzed. The knee-jerks and ankle-jerks were absent. The plantar reflexes and the abdominal and the epigastric reflexes were not elicitable. The sensory disturbances showed an analgesia extending to the umbilicus. The upper extremities seemed to be quite normal.

The pupils were circular, they responded to light and accommodation, and the ophthalmoscopic examination showed the optic nerves to be of normal appearance.

The respiration was short and diaphragmatic. Examination of the chest revealed sonorous and sibilant rhonchi over both lungs, most marked in the upper portion of the right lower lobe. On percussion there was moderate dulness over the lower half of the right lower lobe. This was taken to indicate bronchopneumonia. The temperature was 102°; the next day it was 104°, and the following day 106°.

A blood examination on his entrance to the hospital showed a

marked leukocytosis, and the differential count revealed a remarkable variety of young neutrophilic types of cells. There were very few normal constituents.

The polymorphonuclear leukocytes of normal type were few in number. A considerable quantity of myelocytes and eosinophiles were to be seen. A few nucleated red cells were found, the cytoplasm showing evidences of polychromasia; the great bulk of cells was made up of large diffusely stained mononuclear cells, apparently types of myelocytes.

The following day the blood examination showed the following: Hemoglobin, 70 per cent.; red blood cells, 3,776,000; white blood cells, 28,800. Differential count: Neutrophiles, 50 per cent.; eosinophiles, 16 per cent.; large lymphocytes, 14 per cent.; basophiles, 0 per cent.; small lymphocytes, 10 per cent.; transitionals, 10 per cent.

The red blood cells showed a profound polychromatophilia, Auer rods, anisocytosis, a few with nuclei. The white blood cells showed various myelocytes and an eosinophilia and many irritation forms.

Examination of the cerebrospinal fluid showed that there was a great excess of globulin, no cells, a negative Wassermann reaction, and negative Fehling. The urine was practically of normal condition. The Wassermann serum reaction was likewise negative.

It was noted at this time that the spleen could not be palpated, nor could any area of splenic dulness be determined on percussion. The patient complained constantly of pain in the region of the spleen.

The next day it was noted that over the bases of both lower lobes posteriorly the percussion note was somewhat dull. Anteriorly the percussion note was higher pitched over the right than over the left side. The respiratory sounds over most of the right lung were short in duration and feeble in character. The patient's cough was weak and ineffectual. The pulse was weak and rapid, at times irregular and intermittent.

The next day the patient died, with all the manifestations of a vagus inadequacy and pulmonary edema.

It was evident from the blood findings that, irrespective of the objective signs indicative of a transverse lesion of the spinal cord, what the disease really was could only be explained by some grave disorder of the blood primary or secondary to an undetected infection. A blood culture gave no growth. The blood condition was considered a serious one upon finding the various myelocytes, and because of the presence of young neutrophiles, which were the closest relatives of the myelocyte of the same granulation that we had ever seen. The finding of these cells only reflects upon the strenuous call of the organism to replace the damaged cells, and is to be considered as the early productive phenomena of body resistance. The gravity of the situation from a hematological

point of view was not the myelocytes nor the young neutrophiles, but the secondary changes as shown by the degenerated red cells. Although hematologically such a blood picture cannot be classed among myelogenous leukemias, nor as the acute variety of this disease, in view of the fact that the large number of young neutrophiles constituted the chief feature of the blood anomaly, we believe it justifiable to classify this blood as a new hematological entity, and for the want of something better would designate it as a promyelocytic leukemia containing promyelocytes, as described by A. Pappenheim in his work on *Human Blood Cells*, as well as by one of us (D. M. K.) in the *Folia Hematologica*, 1909, vol. vii.

Even an authority like Grawitz is unable to disentangle the knotty question of the various leukemias. He is forced to declare that the opinions concerning the morphology and pathology of this blood picture are so varied and so rich in exceptions that this last distinction, lawlessness, is perhaps the chief diagnostic feature in this anomaly. We, therefore, do not hesitate in advancing our blood formula as another exception, and deem it permissible to designate the leukemia as promyleocytic.

As emphasized before, there is no separate hematological change to be encountered among diseases of the nervous system. The deviations from the normal in the blood in these diseases, with the exception of lead palsies, belong to the hemopathology of secondary anemias.

Secondary anemia is the outcome of prolonged suffering, and its severity is consonant with the degree of malnutrition. Blood changes that may be directly held responsible for the production of nervous disorder are extremely rare indeed. Case V, which we cite in this communication, is one of this kind. The mechanism producing the transverse myelitis is shown by the pathological findings in the cord. It is more or less of a speculation to explain the etiology of the blood disorder. It is, however, not unsafe to regard an infection as responsible for its production. In this case, particularly, the grave infection overwhelmed the hematopoietic apparatus which hurried to defend the organism by putting out a large force of young phagocytes. It was pointed out by one of us[6] that the most potent leukocyte from the phagocytic point of view is the young representative of the neutrophiles. This cell is capable of engulfing nearly twice as many staphylococci as any other cell. Hence, when a large number of these cells are encountered, it is logical to conclude that their presence is for phagocytic purposes—in other words, an infection is present. Together with full-fledged eosinophilic and neutrophilic myelocytes, as well as the hyperleukocytosis, an ordinary infective

[6] New York Med. Jour., April 13, 1907.

leukocytosis is out of the question, and the condition in our opinion can only be classed among the leukemias, and in view of the presence of the young elements mentioned, the name promyelocytic leukemia is in order.

The significance of the eosinophilia in the case of mediastinal and pituitary tumor is of statistical value only. The origin of the eosinophiles, or rather the stimuli that are responsible for their formation, is still a question to be answered by the experimental hematologists. The interesting work of Opie on this subject may throw some light upon their nativity as well as upon the substance from a chemical point of view, necessary for their increase in the peripheral blood.

A CASE OF BANTI'S DISEASE: SPLENECTOMY FOLLOWED BY TYPHOID FEVER AND APPENDICITIS.

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A considerable number of cases of Banti's disease have already been published and numerous reports of splenectomy performed for the relief of the symptoms of this disease are on record and favorable results have been ascribed to this operation. Although patients who have suffered from this disease and have been apparently cured by splenectomy remain in good health for years, there is hardly anything known of the behavior of these splenectomized individuals during attacks of infectious diseases.

The case of Banti's disease which I wish to present was successfully treated by splenectomy and passed through an attack of typhoid fever one year and a half after the operation. During the course of the typhoid it was necessary to remove the appendix owing to the occurrence of a suppurative appendicitis. It is chiefly on account of the reaction of the splenectomized patient to these infectious diseases that sufficient interest is attached to this case to justify recording it. The existence of syphilis in this case, as shown by the positive Wassermann reaction and by other evidences pointing to hereditary lues, is also of importance.

The following is a brief history of the case, which was referred to me through the courtesy of Dr. William E. Beardsley.

L. G. H., aged seventeen years, female; native of the United States, of German parentage; single, no occupation; admitted to the Jewish Hospital of Brooklyn on January 25, 1909; discharged February 7, 1909. Family history does not offer any significant

facts. She had measles, mumps, and whooping cough in childhood, and some eye trouble three years prior to admission to the hospital; no alcoholic history; only menstruated once eight months before admission and never since. Her present illness dates back five years. She noticed a mass in the upper portion of the abdomen, which was painful at times, especially on pressure, which continued to increase in size. At the same time, she noticed a progressive weakness and loss of energy. She suffered from dragging sensations in the abdomen, slight jaundice and itching, and occasional attacks of epistaxis.

The physical examination showed an undersized, imperfectly developed girl; sclera of slight yellowish tinge; conjunctiva pale; pupils equal and reacting normally to light and accommodation. An examination of the throat did not show anything abnormal; the tongue was moist and clean. The heart was normal to percussion; apex beat was not visible nor palpable; there was accentuation of the second pulmonary sound and a clicking second sound at the apex. The pulse was rapid, soft, and easily compressible. There was dulness from the level of the tenth dorsal vertebra on both sides posteriorly and diminished tactile and vocal fremitus and diminished respiratory sounds. The liver dulness reached from the upper border of the fourth rib to $7\frac{1}{2}$ cm. below the costal margin at the mammary line. The lower border of the liver was easily palpable at that location. The lower border of the spleen was palpable about 9 cm. below the free costal margin. Its notch could be felt two fingers' breadth from the median line, about 6 cm. below the costal arch. The whole abdomen was distended and a diastasis of the recti muscles allowed a mass the size of an orange to protrude just below the ensiform cartilage. The submaxillary glands and the inguinal glands were very slightly enlarged. There was a slight icterus. The hair in the axillæ and around the pubes was scant. The reflexes were normal. There was some ascites, but no edema of the lower extremities. The urine was free from albumin, sugar, and casts; acid; specific gravity 1010. The feces showed nothing abnormal. The Wassermann reaction was strongly positive. The test was made by Drs. Noguchi and Lintz.

The blood examination showed: Red blood cells, 3,200,000; hemoglobin, 48 per cent; leukocytes, 5500; polynuclears, 61 per cent.; lymphocytes, 39 per cent.; eosinophiles, less than 1 per cent.

The specific treatment, which was thorough, and included intramuscular mercurial injections, was not followed by any favorable results, nor was the application of the *x*-rays and the administration of the arsenical preparations of any benefit to this patient.

The temperature curve during her two weeks' stay in the hospital showed only slight rises, reaching at times to a little over 101°. Her pulse varied from 76 to 110, her respirations from 20 to 35 in an irregular way.

The condition of the patient becoming gradually worse, splenectomy was decided upon and was performed by Dr. Walter C. Wood, at the Brooklyn Hospital, on April 26, 1909. The spleen weighed 1 pound 11 ounces, and measured 8 by 4 by 3 inches. It was of moderately soft consistency; there was an area $1\frac{1}{2}$ inches in width at its upper portion, which was soft and semifluctuating. There were numerous whitish areas, which on section showed a cheesy appearance. A microscopic examination showed caseation and giant cells.

From the time of the operation improvement was rapid and continuous, and when she came under my observation again, on September 26, 1909, she appeared to be in a decidedly improved condition. The blood examination the following day showed: Red corpuscles, 5,300,000; hemoglobin, 68 per cent.; leukocytes, 12,800; polynuclears, 58.3 per cent.; lymphocytes, small, 35.5 per cent.; large, 0.04 per cent.

On December 12, 1909, the blood count was: Red corpuscles, 6,160,000; hemoglobin, 65 per cent.; leukocytes, 11,400; polynuclears, 61.5 per cent.; lymphocytes, small, 35 per cent.; large, 2.1 per cent. The eosinophiles were always less than 1 per cent.

There was, therefore, a very remarkable improvement in the condition of the blood, only the percentage of hemoglobin remained comparatively low, while the number of red corpuscles came up to and slightly above the normal limit. The leukocytes increased decidedly in number and came rapidly up to the normal percentage. The relative proportion of the polynuclears to the lymphocytes did not show any marked changes before and after the splenectomy; the eosinophiles were not increased in number.

The patient remained in apparently good health until October 1, 1910, when she was taken with typhoid fever and was placed under my care at St. Catherine's Hospital on the eleventh of that month. The attack was of medium severity; the Widal reaction was strongly positive. The temperature curve differed in no way from that of a typical typhoid up to the eighteenth day of her stay at the hospital, October 28, when a gradual rise of temperature occurred, also a rise in the pulse and respiration, with the setting in of an appendicitis.

October 13, 1910, two weeks after the onset of the typhoid fever, the blood examination was as follows: Red corpuscles, 4,100,000; hemoglobin, 75 per cent.; leukocytes, 4500; lymphocytes, 21 per cent.; polynuclears, 70 per cent.; mononuclears, 7 per cent.; eosinophiles, 2 per cent.; color index, 0.8 per cent.

On October 28, 1910, the day of the onset of appendicitis, the leukocytes were 9800, of which 68 per cent. were polynuclears. The temperature rose during the next two days from 101.8° to 105.4°, with a corresponding rise of the pulse to 135. Chills, severe pain in the right iliac fossa, with exquisite tenderness, resistance at that location, the anxious expression on the face of the

patient, and a rise of the leukocyte count to 15,000 on October 30, pointed to a serious involvement of the intestines at the ileocecal region. The operation, performed by Dr. Frank D. Jennings, revealed a suppurating appendicitis and also a large cystic kidney, which was displaced downward and fixed in its abnormal position. The liver was found smaller than normal and the gall-bladder decidedly paler than usual. The patient made a good recovery, her temperature being of the type of a continua, 103° in the evening to about 102° in the morning, until November 7, when it gradually fell, reaching normal on November 12, the thirty-third day of her stay at the hospital. From then on it showed only slightly rises to about 100, and finally remained normal until her discharge from the hospital on December 11, 1910.

On November 1, two days after the operation, the leukocytes fell to 10,500, the polynuclears being 69 per cent.

By November 16, 1910, the blood count showed: Red blood cells, 4,400,000; hemoglobin, 75 per cent.; leukocytes, 9800; lymphocytes, 25 per cent.; polynuclears, 70 per cent.; mononuclears, 3 per cent.; eosinophiles, 2 per cent.

The patient continued to enjoy good health up to the present time and was examined by me on April 10, 1911. Her weight was 99¼ pounds. There was a slight enlargement of the posterior cervical glands on the right side, but no other glandular enlargement. There were no abnormalities about the chest. The liver dulness began at the sixth intercostal space and reaches down about three fingers' width below the free border of the ribs. The liver felt a little firmer than normal and was smooth. At its extreme right a firm irregular mass could be felt, which was most likely the right cystic kidney as found at the time of the operation. The liver dulness at the mamillary line occupied only two intercostal spaces. The upper and lower middle incisors were slightly notched. Temperature, pulse, and respirations normal. No other abnormalities were found.

Blood examination made on April 7, 1911, showed: Red blood cells, 5,860,000; hemoglobin, 104 per cent.; leukocytes, 11,600; polynuclears, 78 per cent.; mononuclears and transitionals, 2 per cent.; lymphocytes, small, 17.5 per cent.; mast cells, 0.5 per cent. Blood coagulated almost immediately on lobe of ear.

The points which are most evident in this case are: (1) A typical clinical picture of the disease described by Banti, Senator, and others, namely, splenomegaly; the decidedly enlarged liver; the typical blood findings; the slowly progressive exhaustion were well pronounced in this case. (2) The lack of development of the patient, her appearance being that of a child aged twelve years. (3) The positive Wassermann reaction. (4) The rapid improvement in the condition of the blood, with a decided improvement in the hemoglobin following the operation of splenectomy, but not reaching

the normal, and remaining practically stationary for at least nine months, varying from 63 to 78, while in the recent examinations it reached even above normal, 104 per cent. (5) The typical characteristic typhoid, differing in no way from that of patients not operated on, with the exception of the blood findings, which showed a rather high leukocyte count for a case of typhoid and a relatively high polymorphonuclear leukocytosis. (6) The reaction to the surgical interference during the course of the typhoid did not present anything characteristic, and her recovery was as rapid as one could expect in a patient not splenectomized.

The internal secretion of the spleen, which according to modern physiologists[1] activates trypsinogen into trypsin, is either supplied in this case by a supernumerary spleen or spleens, or else is effectively substituted, perhaps, by the succus entericus. At any rate, the proteolytic digestion and metabolism is not deranged.

This case further demonstrates that the enlargement of the spleen in typhoid is not essential to the elaboration of immune substances, again assuming that there are no supernumerary spleens.

There is a possibility that hereditary syphilis and tuberculosis of the spleen form etiological factors in this case, as shown by facts previously stated. Evidences of gastro-intestinal diseases could not be obtained. Willi Schmidt's[2] case, recently published, is that of a boy, aged fourteen years, with retarded development, presenting Banti's disease symptoms and having a positive Wassermann reaction, which was successfully treated by salvarsan injections. In 2 out of 3 cases of Banti's disease recently treated at the Jewish Hospital, of Brooklyn, there was found a positive Wassermann reaction.

Marchand[3] and Chiari[4] reported the presence of hereditary lues in some cases of Banti's diseases. Other cases fail to present any evidence of lues. In the carefully observed case of Emmanual Policek[5] there was a negative Wassermann reaction. The pathological condition was designated as chronic inflammation with connective tissue proliferation and the formation of granulomata, closely resembling tubercles. There were, however, no tubercle bacilli found after splenectomy.

The etiology is still obscure. The success of splenectomy places the chief seat of the disease in the spleen. So much can be conceded at present from the considerable number operated upon, to which the one under consideration may be added.

It is also clear that a toxemia emanating from the spleen is responsible for most of the symptoms observed in these patients. In the cases of this disease that came under my observation, the hemor-

[1] Schiff, Herzen, Gachet, and Pachon.
[2] Münch. med. Woch., March 21, 1911, p. 625.
[3] Ibid., 1903, p. 11.
[4] Prager med. Woch., 1902, No. 24.
[5] Folia Hematologica, 1910, ix, 508.

rhages were most readily accounted for by a toxemia. Neither engorgement of the portal system nor direct pressure on vessels through enlarged intra-abdominal glands seemed to offer a satisfactory explanation for the occurrence of these often severe hemorrhages, while the resemblance to those of undoubted toxic origin was apparent. In one of my cases of this disease hemorrhages occurred early, when there was only very moderate splenic enlargement and no evidence of any involvement of the liver. Is it possible that an excess of internal secretion of the spleen is responsible for the occurrence of the symptoms, such as one observes in that of the thyroid gland? Or is this toxic substance formed through the agency of infection? Sippy[6] found that filtered splenic juice obtained from patients suffering from Banti's disease injected into rabbits caused death in a few hours.

Sciolla, on the other hand, in a similar experiment with splenic pulp failed to observe any apparent effect. Umber found an increased destruction of the albuminoids in this disease, while Arthur Müller[7] found normal metabolism in his case.

In conclusion, I wish to emphasize the remarkable results following splenectomy in my case; the lasting improvement and the ability to combat severe infections. Also the restoration of the blood to the normal condition as to the formed elements and to a marked increase in its coagulability.

REMARKS UPON SOME PHASES OF THE SPASTIC-PARETIC SYNDROME OF CEREBRAL DIPLEGIA.[1]

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If we are to make any signal advance in the treatment and prevention of the spastic-paretic syndrome of infantile cerebral diplegia, we must proceed upon the sound anatomical and physiological laws underlying this disease. At the outset it should be emphasized that infantile cerebral diplegia is not a disease entity, but has a clinical basis only.

It has been stated authoratively that there is a description of Little's disease in Audry's treatise on orthopedics, published in 1741, and that Delpech incidentally published a single case in 1728. But the condition must have existed from the remotest antiquity, and there is no doubt that a careful research into the past, both in

[6] Amer. Jour. Med. Sci., p. 428.

[7] Münch med., Woch., 1909, No. 45, p. 2316.

[1] Read before the New York Neurological Society, February 6, 1911.

medical and graphical records, would reveal further evidence of the condition. While this statement might not hold good for Little's disease, *per se*, as an accident of childbirth, we should consider the frequency of spastic states in hysteria of young girls and admit that such cases might easily be confounded with organic disease originating in early childhood. In 1840 Heine, the pioneer worker in poliomyelitis, anticipated Little by giving a good description of the syndrome, which, however, he named "spastic cerebral paraplegia." This discovery in nosography probably passed unnoticed; just as happened when Little, in 1861, published his classic account of the syndrome which now bears his name. Many of the points elaborated by Little had to be rediscovered later; showing that the medical world did not really assimilate Little's work until years after its publication. The reason for this lack is not far to seek. Little's syndrome was looked upon at first as an obstetrical subject; it then became an orthopedic subject; today it is admittedly a neurological subject. It is, however, an excellent illustration of a borderland disease, and these disorders are almost invariably neglected, and viewed from a partisan standpoint. Fortunately several of the most popular German journals consider only these borderland subjects, whereas American medicine has been very slow in adopting this practice, and therefore lacks much in harmonizing and bringing up to date our knowledge of many subjects.

Some years after Little's publication Erb and Charcot independently described a form of developmental spasticity of spinal origin. The mental state in such cases was, however, normal, hence the cerebrum was supposed not to have been involved. Today we know that Little's syndrome may be due to an intracranial infection, and yet the intellect may be unaffected. On the other hand, the number of cases of spinal spasticity in children recorded in the literature is steadily multiplying. The syndrome follows or accompanies many injuries and diseases of the medulla and its membranes. Naturally, from the beginning much controversy has arisen as to the respective parts played by the brain and spinal cord in these cases. Such a controversy led still to others: What was to be understood by Little's disease? Should it comprise other forms of rigidity or spasticity in childhood, including double athetosis and congenital chorea? Should one believe that the brain and spinal cord might be individually injured in labor, with the production of two syndromes?

As intimated above, and as still holds true in our day, some writers could not dispossess themselves of the idea that injury of the brain must be accompanied by idiocy and *vice versa*. In searching the literature of our subject one must bear this obsession constantly in mind. Inasmuch as spasticity was commonly associated with high degrees of mental defect, the account of Little's disease has been much overcharged.

In attempting to explain the spasticity of cerebral diplegia, it is

not, therefore, surprising that two views soon came into prominence: (1) The dualistic, which makes of the results of cerebral and spinal accidents two different diseases; and (2) the unicistic, which, eliminating all spinal cases from causes *in loco,* insists that a cerebral element is invariably in evidence in Little's syndrome, and allied states. Marie, one of the earliest writers on the subject, believed that the so-called spinal cases were really due to vices of development, and that they occurred with special frequency in premature children. To him we are especially indebted for bringing out the fact that an affection in the pyramidal tract, throughout any part of its course, might at least in its early developmental growth, lead to a common result. Hence subdevelopment, or a lesion anywhere in the cerebrospinal center which comprised the pyramidal tract, might be held responsible for Little's syndrome. Thus, given a lesion high in the motor area of the brain, we should expect coincident idiocy, epilepsy, etc., and if the lesion occurred in the lower part of the pyramidal tract, the symptoms would vary accordingly in range and degree of spasticity and mental deficit. Marie's views would seem to solve our difficulties completely were it not for the fact that in many cases of diplegia, to be mentioned later, there exists no demonstrable lesion anywhere throughout the pyramidal tract. Physiologically, as we shall see later, Marie's views may not be so incorrect after all. In passing, it is of considerable interest to note the summation of Van Gehuchten's elaborate study that a premature birth, by reason of the subdevelopment of the nervous system, must impose a very different condition from a difficult labor with its attendant asphyxia, yet he leans to the spinal view in causation of spasticity, a theory hard to consider, much less understand.

The unicistic view makes of Little's disease a cerebrospinal affection, the spinal phenomena being a result of the cerebral disease. If one accepts this view the syndrome offers infinite variety—spastic paraplegia, generalized rigidity, double athetosis, congenital chorea, etc. But some would exclude from this picture all hemiplegias, whether of one side or both sides. Raymond was one of the first to grasp the idea that spasticity and paralysis are equivalents, and may replace each other or be found side by side. Earnest attempts have been made for several years to do away with the term Little's disease as such, and speak of it as Little's syndrome or the spastic-paretic syndrome. To such workers it is a matter of the insufficiency of autopsies, not of clinical material (Déjerine, 1903).

The idea is not without point when we consider that in the current literature the syndrome has its index, even in its simplest classification, under the headings of general muscular rigidity of cerebral origin, paraplegic rigidity, double spastic hemiplegia, double athetosis, and generalized congenital chorea. It is not a

little surprising to find from actual analysis of all the classic material of our subject at hand, that the true and typical development of Little's syndrome requires there shall have been a prematurity of birth as well as an asphyxia, and in this manner the undeveloped pyramidal tracts become unduly compressed (Baudon).

In an analysis of 38 cases of asphyxia at term, 11 showed paraplegia, 15 generalized rigidity, 7 transitional forms, 2 hemiplegia, and 3 athetosis and chorea. The small incidence of cases in such a common accident as asphyxia at term has prompted a question whether there was not an antenatal toxemia present, such as tuberculosis or syphilis. The autopsy findings in 44 collected cases showed 24 with general rigidity, 9 with spastic paraplegia, 3 with unilateral spastic hemiplegia, 2 with spastic diplegia, and 5 with double athetosis. Of the 24 cases of generalized rigidity, the brain was normal in 6, the cortex was atrophied in 5, there was porencephaly in 3, adherent pia in 3, thickening of dura with or without adhesions in 4, hydrocephalus in 2, microgyria in 1. The cord was normal in 6, while in the other 18 it showed arrested development or sclerosis of the pyramidal tracts. The cases of double athetosis were not included. In the 9 cases of paraplegia there was atrophy of the convolutions in 3, hydrocephalus in 2, porencephaly in 2, and meningo-encephalitis in 2. Generally speaking, all these lesions were associated with agenesis of the pyramidal fibers. It will occasion no surprise if we attempt no conclusions from this limited data, other than that the pyramidal tracts may be perfectly intact despite the presence of spasticity (Spiller, Speilmeyer, Rolly, Déjerine, Hausholler, Collins, and Rhein). This fact is of no mean importance and well compensates us for citing statistics at this time.

Furthermore, at autopsy it is not possible to differentiate a paraplegic brain from a diplegic, nor a diplegic from a choreic or bilateral athetosis, nor can we differentiate a diplegic from a double hemiplegia. One must admit in passing that there is still great confusion in the nosology of the disease, owing to the fact that complete and modern studies of the entire brain are rarely made in idiot asylums in any country, a neglect which renewed interest in the whole problem of developmental defects in such children should remedy at no distant date. The brain in many cases of the spastic-paretic syndrome of diplegia, apparently showing little or no change to the naked eye, might easily show agenesis in microscopic study. We should not forget, however, that even agenesis is not essential for the production of Little's syndrome, for a lesion anywhere in the motor path below the cortex may produce the same result. It is also well known that a similar breadth of variation may occur in infantile hemiplegia. A similar mechanism of degeneration of the neuron is supposed to account for the senile spasticity without evidence of gross lesion, as in senility where an intracortical pathology is postulated.

In a study of the atypical forms and variations of the spastic syndrome, especially in connection with agenesis, one is confronted with a steadily increasing number of cases of the hereditary, familial type of the disease. Some writers have described it purely as a form of spinal agenesis, but there is plenty of evidence that an analogous condition of cerebral origin also exists, although it does not ascend much above the decussation of the pyramids. In still a third class of cases both the brain and cord are found fully intact. In all these cases, however, lesions when found are seated low in the brain. It is not surprising to note that complete cerebral and spinal analysis at autopsy frequently reveals nothing to account for the condition. The lesson we learn from this type in reference to the spasticities is that there is not always evidence of the causal factors of Little's syndrome, and in a possible majority of cases there is no organic disturbance to be found even with the microscope. The affection is, therefore, probably a true neurosis.

In sharp contrast to this view of looking for a definite organic basis for spasticity, the recent work upon the variant forms of pseudotetany needs to be considered. Two recent American writers, overwhelmed, so to speak, by the wealth of material on spasticity and the extreme limits of the etiology, have endeavored to bring the entire syndrome under this head. If we follow up the subject carefully under its enormous literature, we are surprised in the frequency with which the pseudo type occurs in the disorder of the central nervous system known as the persistent spastic myotonia of Hochsinger, or, better, as the pseudotetany of Escherich. It is supposed to depend upon a form of dry meningitis. There is this parallelism between pseudotetany and Little's syndrome: there is no necessarily central lesion in either, and pseudotetany is sufficiently common in many forms of encephalitis, chronic hydrocephalal, and other brain lesions. While ordinary tetany may be due to a toxemia, pseudotetany must be otherwise accounted for. Many of its descriptions shade into conditions which Escherich has shown to be not unlike the Little syndrome. We find many undiagnosticated conditions of cerebral spasticity in children described as Little's disease which would more properly be termed pseudotetany. If we compare the two conditions, they are not so dissimilar in clinical manifestations. Space forbids a consideration of this analysis here.

One of the most interesting and instructive phases of our subject is the combination of spasticity and flaccidity in the same case. This type was not long ago thought to be rare. Indeed, Förster discussed the subject last year in an extensive paper. Most of us would hold it an axiom that spasticity from its very nature cannot exhibit flaccidity, and that a true association of the two would be extremely rare and anomalous. I have demonstrated, however, in my service of more than 200 cases at the Randall's Island Insti-

tution that this association may be shown in many cases, and that the ratio between the two conditions has a wide variation to different tests. Thus, some spastic muscles may show unusual weakness, and the flaccid types of muscle may be made to show spasticity. Many cases of the preponderating flaccid type may be also combined with ataxia. The absence of cerebellar lesions in the few cases of this type which have come to autopsy makes the understanding of these cases difficult indeed.

The flaccid and mixed types have the same etiology and pathological changes as the classic spastic cases. The typical flaccid paretic types cannot stand or walk, and never learn to do so. There is a notable absence of muscular resistance, and the muscles can be stretched without pain. The joints even can be flexed or extended beyond their normal limits. The electric reactions are normal, but there is some form of voluntary motion, although the movements are purposeless. The limbs can be moved with great activity in some cases, and the reflexes in many cases are normal. Most of these children show evidences of severe cortical lesions—defects of intelligence, aphasia, and not infrequently convulsions. Here and there, in addition to spasticity, choreic movements and strabismus are also in evidence. One of Förster's cases had an opisthotonos of the neck and back. In one of these flaccid cases Förster has reported a Babinski reflex, distinct spasticity and heightened reflexes. Most of the spasticity in these cases is developed in looking for resistance. In the few cases that have been autopsied the forebrain has been found atrophic and sclerotic; this fact enables us to understand, in part at least, the ataxia and incoördination developing on the extreme hypotonus. One is often so engrossed in studying the typical phases of spasticity in cerebral diplegia that these unusual flaccid, atonic-astatic cases, as Förster calls them, have been overlooked and neglected. Careful study of them in the near future must throw a flood of light on the genesis of spasticity.

Inasmuch as anatomicopathological research has been so barren in fully explaining the spastic-paretic states of cerebral diplegia, we may profitably turn our attention to the physiological studies upon this disorder. These we find largely in the German school, and more especially in the work of Förster.

It is most important for us to recognize that the main descending paths of conduction from the cortex to the spinal cord are the pyramidal tracts, although the extra-pyramidal tracts play a role in the sequent spasticity from pyramidal tract disease. Two components are in evidence when an interruption occurs in the pyramidal pathways. The first is a corticospinal impulse sent through the pyramids to the anterior roots and to the muscles, which increases tension and induces contractions. Many static and kinetic disturbances follow an interruption in this corticogenic

impulse. This kind of motor disturbance may be termed the paretic component. Hence an acute interruption by destruction or great irritation of the pyramidal tracts in the internal capsule causes the well known hemiplegic syndrome. The failure of this corticogenerating impulse accounts for the spontaneous resolution in the paralyzed muscles, or, if the hemiplegia develops slowly, the muscle movements are greatly limited in range and degree. In the legs, for instance, there can be no marked voluntary dorsal flexion of the foot, flexion of the thigh, outer rotation and abduction of the thigh. The opposite movements may be performed a little better, but here, too, the range and freedom of individual movements are likewise affected. The manner in which spontaneous restitution occurs in these cases is in no small part bound up with the intact direct pyramidal tracts, and the homolateral accessory paths which, under automatic control, and even under some voluntary control, are capable of increased development by exercise and special mechanical therapy.

The absence of muscular tension generated from the cortex, as shown in hemiplegics, is not only in evidence by a loss of voluntary motion, but is also seen in the presence of involuntary action both of a static and kinetic character. Thus, there is a defect in contraction of the dorsal flexors of the foot, especially the extensor digitorum and the flexors of the leg, and there is also a defective tension of the extensors and adductors of the pelvis and flexors of the knees, hence the peculiar "scissors" gait of diplegics. These combined defects are much more pronounced when they involve the upper extremities, since the fingers are highly specialized in complex movements.

In the spastic-paretic syndrome of diplegia the duplex lesions in the cortex cause a loss of segmental movements in the limbs. While interruption of the pyramidal path abolishes or diminishes the corticogenic excitability of the muscles, the peripherogenic excitability increases it. Here we see that the peripheral excitability acting either through spinal or subcortical centers outranks even the inhibitive influence of the pyramidal tracts. For even in complete destruction of the pyramidal tract the peripherogenic influence may cause spasticity in flaccid muscles, independent of cortical inhibition. This is proved clinically in the rare flaccid type of cerebral diplegias in which spasticity may be shown by developing a strong peripherogenic impulse in examining old contractures, a fact taken advantage of in the training of such cases and in those spastic cases rendered flaccid by dorsal root section.

We thus come back to the twofold make-up of the pyramidal bodies, which contain inervation fibers which transmit tension impulses and inhibitory fibers which preside over spinal cord reflexes. The tension impulse is a continuous one, antagonizing the steady stream of peripheral impulses, so that the latter are held in check.

These conceptions are the only ones adequate to explain that with sudden interruption in the pyramidal paths, special reflex activity is gradually increased. Certainly, the old idea that progressive development of imperfect pyramids in infancy creates a physiological irritation or tension is no longer adequate in the light of clinical and pathological facts. Further corroboration of the newer view is shown in that, as a general rule, the more destruction of the pyramids there is in diplegia, the less voluntary motion there is, likewise the increase in flexor reflexes is found. However, this is not invariably true in all cases of paraplegic types of infancy.

The enhanced spinal reflex excitability is further shown in that voluntary motion may be accompanied by involuntary acts; thus, voluntary flexion of the leg may be accompanied by involuntary dorsal flexion of the foot. The voluntary act somehow liberates a reflex which becomes an involuntary movement.

A number of instances might be cited to show that some diplegics lose the power of isolated movements. We sometimes see a leg or arm fully capable of involuntary motion because of intact corticogenic excitability, yet in the movements of these limbs one may produce synchronous involuntary movements. The only pathological phase which these muscles under study present is a greatly increased reflex excitability. It is entirely proper to question here whether the acts just described are not overflow impulses passing by extra pyramidal tracts, or, still more pertinent, an affair of the lower peripherospinal reflex. It is certain, however, that these involuntary associated movements are subcortical in origin and explanation. Separate intracortical reflex centres are not necessary, as some of the French school have elaborated.

The abnormal involuntary tension which appears in diplegics when their muscular insertions are approximated is due to the increased reflex excitability of the muscles. Curiously enough this spastic muscular contracture is not seen in many cases at first, but as soon as the insertion points are approximated a few times or allowed to remain so awhile, involuntary tension quickly appears. In a few weeks even old stationary cases may be converted into irreducible spasticity. Here, at least, orthopedic alarm is justified. Muscle atrophy, too, quickly succeeds in these neglected cases, a curious fact worthy of further study.

While spastic contracture is only a product of an extreme degree of heightening the normal muscular tonus, the manner in which this is brought about is a very complicated, interacting, subcortical mechanism. The lesion of the cortex inducing the morbid train of causes in the spasticities of cerebral diplegia is but the simplest part of the postulate. Under normal conditions we see an involuntary reflex process called forth by peripheral sensory irritants which arise in the joints, tendons, ligaments, and especially in the muscles at the moment of approximating the insertion points.

The impulse passes along the sensory nerves and posterior roots into the gray matter of the cord, whence it is again transmitted to the muscles. It is always under the inhibitory control of the superior pyramidal tract acting on the spinal nuclei of the muscles. Thus, the conflict in the spastic-paretic state of diplegia is a three-cornered one, lying between the amount of corticogenic tension impulse, the peripherospinal reflex, and the inhibitory control from the cortex through the partly destroyed pyramidal tracts.

The chief phenomena by which the spastic-paretic state of muscle in diplegics is to be recognized are: (1) Increase of tendon reflexes; (2) increase of skin, periosteal and soft part reflexes; (3) the appearance of extensive and intensive involuntary associated movements in connection with definite voluntary movements, which, in turn, may even amount to impossibility of isolated movements; and (4) spastic muscular contracture (Förster).

We must remember however, that the inhibiting function of the pyramids is throughout independent of the influences which cause muscle contracture, for there are many cases of inhibition without contracture and *vice versa*. But in the great majority of cases the inhibiting function is in evidence. The inhibiting function of the pyramidal tracts suffers earlier and more frequently than any other; in other words, it may be counted more vulnerable than the increased reflex activity of the muscles and the paresis of the voluntary muscles. The above view is enhanced when we remember that with few fibers spared to the pyramidal tract anywhere in its cerebrospinal path, the amount of corticogenic impulses capable of being generated may be fairly amazing. The possibility that many such impulses are transmissible by extra pyramidal tracts and by the homolateral fibers must be thought of and studied. All possible variations of transmission of corticogenic impulses are needed, however, to explain the association, often side by side in the same case of some voluntary motion, some flaccid palsy, and a certain amount of spasticity.

This field is worthy of continued, painstaking study from all sides. It is only by such work, clinical, experimental, and pathological, that we can hope to arrive at any rational therapeutics for the spastic-paretic states of cerebral diplegia.

ATHEROSCLEROSIS, WITH SPECIAL REFERENCE TO THE PHYSIOLOGICAL DEVELOPMENT AND PATHOLOGICAL CHANGES IN THE INTIMA.

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The present paper is based on the microscopic study of the vascular system of 20 cases selected from about 300 autopsies studied in Berlin and Munich during the spring and summer of 1908.

The material was selected with the object of studying the physiological development, as well as the pathological changes occurring in the vessels from infancy to old age, and while not as complete as might be desired in late adolescence, yet the essential changes are fairly well covered.

The vessels usually selected for microscopic study were the aorta, pulmonary, renals, splenic, coronaries, præfossæ Sylvii, and in many cases various others.

For the physiological studies these were often cut both longitudinally and transversely, in order that the details of structure might better be made out.

The material was fixed in 2 to 10 per cent. formol for a day or so, and then sectioned with the freezing microtome, after which the sections were preserved in distilled water until stained, which was usually on the following day.

Carmine or hematoxylin were chiefly used as nuclear stains, the former usually combined with Weigert's elastic stain and the latter with Sudan III for fatty degeneration.

Protocols of each case, containing the age, sex, clinical diagnosis, and gross pathological changes, were made at autopsy.

In the study of the sections an exact description of the objective findings in each tunic, with the various stains, was dictated at the time of examination, but the limits of this paper preclude more than the briefest abstract of what appear to be the more important points.

Case I.—Male, aged five months. Cause of death unknown. Nuclear stains of the aorta, subclavian, and carotid show the intima to consist chiefly of polymorphic connective tissue cells. In the superficial layer, where the intima is slightly thickened, are a few clusters of round cells. A definite elastic lamella with very slight fissions containing a few apparent muscular cells separate intima and media.

Case II.—Male, aged eleven months. Died of ileocolitis. Sections of the descending portion of the arch of the aorta show the clastica interna to consist of a deeper, well-defined lamella, and a superficial, less compact, parallel layer, between which is a longitudinal muscular band. The common iliacs show slight fission of

the elastica interna containing longitudinal muscular elements. The larger splanchnic arteries show, likewise, splitting of the elastica interna into two or three layers with cellular inclusions of a muscular or connective tissue nature.

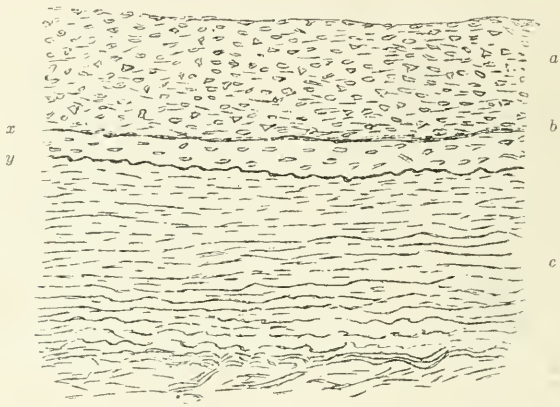

FIG 1.—Longitudinal section of the aorta of Case II, a male, aged eleven months. In this and the subsequent drawings *a* represents the connective-tissue layer of the intima; *b*, the longitudinal muscular layer of the intima; *c*, the media; *x*, the elastic marginal stripe, and *y*, the elastic marginal lamella; both developed with the inclusion *b* from the original elastica interna.

CASE III.—Male, aged three years. Died of milliary tuberculosis. There is a small area of fatty degeneration in the superficial layer of the intima of the aorta and a suggestion of a longitudinal muscular layer in its depths. The intima of the pulmonalis consists of a narrow layer of connective tissue cells and a few elastic fibers.

CASE IV.—Female, aged eight years. Died of acute lymphatic leukemia. The intima of the aorta consists of a marginal layer of polymorphic connective tissue enclosing a rather indistinct network of fine elastic fibers, and a deeper longitudinal muscular layer lying between two parallel longitudinal elastic lamellæ. A capillary vessel is seen in the latter coat. The pulmonalis shows no longitudinal layer in the intima, and the elastic fibers of this tunic are very fine. There is some round-cell infiltration in the media and adventitia of these vessels (lymphatic).

CASE V.—Male, aged thirty-one years. Died of aortic insufficiency (syphilitic). There is an organized thrombus on one of the aortic valves, numerous sclerotic plates in the aorta, and pessary-like thickenings around the mouths of the intercostals. There are fatty spots on the coronary intima and the renals appear thickened. The depths of the sclerotic plates show fatty and calcareous degeneration. These thickenings show both connective tissue and elastic tissue increase. The musculature of the media is in some places almost completely destroyed by perivascular connective-tissue formation.

The intima of the renals shows proliferation of the connective-tissue layer, but the elastica interna is distinct, showing only the slightest fissures with connective tissue or muscular cell inclusions.

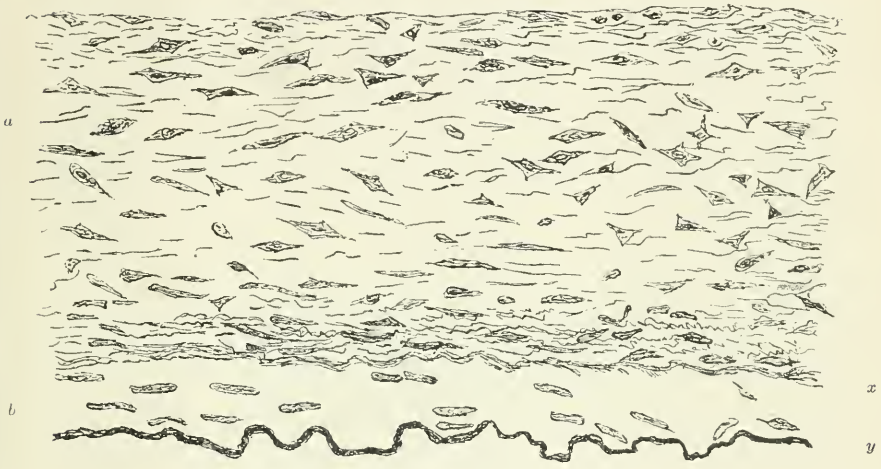

Fig. 2.—The same as Fig. 1, showing only the intima. × 350.

Case VI.—Male, aged thirty-three years. Cause of death unknown. There is extreme hypertrophy and dilatation of the right ventricle, caused by a primary sclerosis of the secondary and tertiary branches of the pulmonary artery. The systemic vessels appear normal. The intima of the aorta consists of a superficial layer of polymorphic connective-tissue cells and fine elastic fibers, a middle layer, consisting of three or four fairly definite longitudinal elastic stripes enclosing a few cells with longitudinal elongated nuclei, and a third layer, bordering the media, consisting of longitudinal muscular and coarse longitudinal elastic fibers. There is slight thickening of the intima of the primary pulmonary artery, but the secondary and tertiary branches show extreme thickening of both the superficial connective tissue and deeper elastic layer, either of which is thicker than the media. The elastic layer is composed of coarse, rather compact elastic fibers enclosing a considerable number of deeply staining cells which appear to be muscular.

Case VII.—Male, aged thirty-three years. Died of peritonitis from carcinoma ventriculi. The aortic intima shows the three layers, but the lamella usually seen separating the longitudinal elasticomuscular coat of the intima from the media is here not well defined, but passes in some places into the elastic framework of the media. The intima of the renals is considerably thickened and the elastica interna shows some fission, with muscular inclusions.

Case VIII.—Male, aged thirty-eight years. Died of cardiorenal disease. The viscera are congested and the kidneys show scars of

numerous old infarcts. The mitral and aortic valves and the aortic bulb show evidence of sclerosis. There are fatty elevations on the intima of the aorta and common carotid, showing no connective tissue increase, a sparse round-cell infiltration, and a granular attenuated appearance of the intercellular substance suggestive of edema or fatty degeneration. There is a longitudinal elastico-muscular layer in the depths of the carotid. A similar layer is seen in the left coronary. The renals are sectioned at their point of bifurcation, where the elastica interna is broken up into two or three different layers, the intervening spaces lodging a few muscle or connective-tissue cells. The other coats of these vessels are normal.

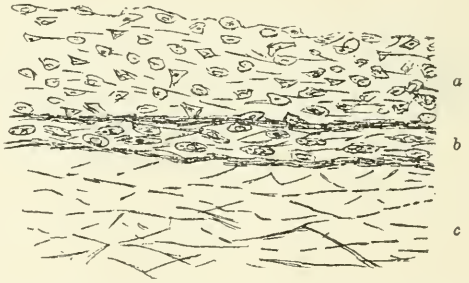

FIG. 3.—Longitudinal section of common carotid of Case VIII, a male, aged thirty-eight years, showing longitudinal muscular layer of the intima developed between the two lamellæ of the original elastica interna.

CASE IX.—Male, aged thirty-nine years. Died of pernicious anemia. The deeper layer of the aortic intima shows what are evidently longitudinal muscular elements. Near the mouth of the celiac the intima consists of a superficial connective tissue and a deep longitudinal layer, the latter disappearing after passing into the mouth of the celiac. The intima of the common carotid is thickened throughout about one-third the circumference of the vessel, and is separated from the media by a distinct elastic layer. There is a slight thickening limited to the superficial layer of the intima at the mouth of the left coronary. There is fission of the elastica interna into two or three layers throughout a part of the vessel's circumference in both renals and the splenic. The media and adventitia of most of these vessels show connective-tissue proliferation and round-cell infiltration, which I believe to be due to the anemic state.

CASE X.—Male, aged forty years. Died of typhoid fever. There are fatty spots on the aorta and pulmonalis which show, microscopically, degeneration of the superficial layer of the intima. The deeper layer of the intima reveals a fatty degeneration of a different type. Here the cytoplasm of the cells shows fatty changes, while the nuclei of some of them are still well stained. The elastic fibers are not

fatty degenerated. The above cells belong to the longitudinal muscular layer.

Case XI.—Male, aged forty years. Died of tuberculous meningitis and pulmonary tuberculosis. The intima of the aorta shows a few scattered fatty patches. There is slight sclerotic thickening around the mouths of the coronaries and the intercostals. In the superficial layer of the intima of the bulb of the aorta and the pulmonalis a few round cells are seen. In the depths of the intima of the aorta a thin longitudinal muscular layer is seen. The elastic elements of this deeper layer of the intima consist of two or three rather distinct stripes which in some places break up into numerous finer layers. The arrangement of the deeper portion of the intima is not so distinct here as it usually is in the descending portion of the arch and the thoracic and abdominal portion. Longitudinal sections of the iliacs show very fine elastic fibers in the connective tissue layer of the intima. The elastica interna consists throughout a part of the section of a single definite lamella, while at other places three or four closely lying parallel layers exist which diverge from each other on approaching the aorta. Sections of the carotid and left coronary show fission of the elastica interna. Sclerotic portions of these vessels show that the thickening is confined chiefly to the tissue lying between these two elastic lamellæ.

Case XII.—Female, aged forty years. Died of diffuse peritonitis from operation for carcinoma uteri. The renals and celiac arteries appeared slightly thickened. The intima of the aorta consists of a superficial connective-tissue layer enclosing fine elastic fibers; a middle, rather loose meshed, fibrous network, with its cell inclusions, separated from the superficial layer by a rather coarse longitudinal elastic stripe, and an external layer consisting of coarse longitudinal elastic fibers and longitudinal muscle cells. There is no elastic lamella separating the intima from the media in the pulmonalis, the two blending insensibly into each other. Both renals and the celiac show fission of the elastica interna, but no connective-tissue thickening internal to this. The splenic shows no such fission in its elastic lamella. There is perivascular connective tissue proliferation and small-cell infiltration around the vasi vasorum in the larger vessels.

Case XIII.—Female, aged about forty-five years. Died in an insane hospital. The aorta shows extensive sclerotic and calcified patches in the intima throughout, most marked, however, in the arch. The absence of atheromatous ulcers with such extensive sclerotic changes justifies, immediately, the diagnosis of syphilitic mesaortitis. Microscopically, the fibrous thickenings in the intima and media, with the perivascular infiltrations and proliferations (Mesaortitis Syphilitica or Periarteritische Flecken), confirm the macroscopic diagnosis. Sections of the renals show very slight fission of the elastica interna. The intima of the right coronary con-

sists of a superficial connective tissue and a deeper longitudinal muscular layer.

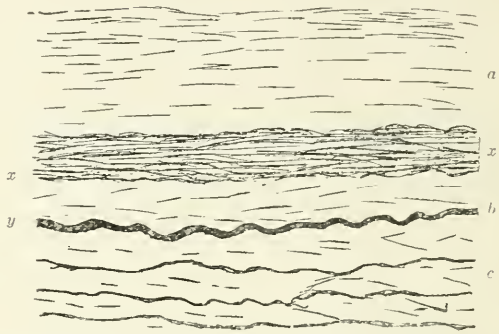

Fig. 4.—The physiological evolution of the elastic elements of the aortic intima. The hyperplastic middle layer developed from the internal lamella of the elastica interna or the elastic marginal stripe is shown at *x*.

Case XIV.—Male, aged forty-six years. Died of purulent meningitis. The aortic bulb, arch, and thoracic portion, the innominate, both carotids, and the subclavian all show sclerotic and fatty spots on the intima. The Sudan stain shows two different processes to exist in the intima of these vessels. The connective-tissue cells of the superficial layer show moderate fatty degeneration of their cytoplasm. The round cells in these areas are not degenerated. The deeper layer of the intima shows much more extensive fatty degeneration. Here in some places the cell structure is completely destroyed and its place occupied by long chains of fat globules. The elastic fibers in this layer are, likewise, undergoing fatty changes, the fat existing in them as the very finest granules, even when studied with the oil immersion lens. The renals show considerable thickening of the connective-tissue layer of the intima, and the elastica interna is split into several layers or broken up into fibers throughout a considerable portion of its course. The splenic shows lamellation of the elastica interna and considerable thickening of the connective-tissue layer. The left coronary reveals enormous thickening of the connective-tissue layer of the intima and the existence of a well-defined longitudinal elasticomuscular layer of the intima. The latter and the deeper portion of the former are extensively involved in fatty degeneration, in both their cellular and elastic elements.

The intima of the larger vessels shows two distinct processes—a superficial fatty degeneration of the connective-tissue layer, probably due to the infection, and an atherosclerotic process, most pronounced in the deeper layer of the intima.

Case XV.—Male, aged forty-seven years. Died from myxosarcoma of the mediastinum. The aorta, coronaries, renals, and splenic appear sclerotic, the coronaries markedly so. The latter

vessels show fatty degeneration of the cellular elements and elastic fibers in the deeper portion of the intima, the latter tunic being markedly thickened. There is only slight fission of the elastica interna, but no distinct longitudinal muscular layer is seen. The renals show no splitting of the elastica interna. The splenic shows considerable thickening of the connective-tissue layer and the elastica is split into two or three layers throughout a part of the circumference of the vessel.

Case XVI.—Female, aged forty-eight years. Cause of death unknown. Mitral stenosis, vegetative endocarditis, multiple infarcts, and sclerosis of the pulmonary arteries characterize the vicious circle in this case. The aortic bulb shows slight evidence of a longitudinal muscular layer in the deeper intima. The connective-tissue layer is distinctly thickened. The longitudinal muscular layer is much more marked in the abdominal aorta. The right renal is normal and the elastica shows only the slightest fissures. The left renal and left vertebral show fission of their elastica interna, and the splenic a considerable thickening of its intima.

Case XVII.—Male, aged fifty-one years. Died from operation for carcinoma of the esophagus. The aorta, femoralis dextra, renals, splenic, and left coronary all appear macroscopically thickened. The longitudinal muscular layer of the aortic intima is not very well developed. The femoral shows pronounced thickening of its intima throughout a considerable portion of its circumference. The deeper layer of this coat, consisting of numerous coarse elastic fibers and cellular inclusions, shows fatty degeneration of both these elements. The elastica interna of the right renal is broken up into numerous fibers at two antipodal points of the vessel. These undoubtedly represent an approach to the point of bifurcation of the vessel. The connective tissue layer of the intima of the left renal is slightly thickened. The splenic shows fission of its elastica interna with inclusion of a fairly well developed longitudinal muscular layer. There is a pronounced eccentric thickening of the intima of the left coronary which involves both the superficial and deeper layer. The fatty degeneration is much more marked in the deeper than the superficial layer.

Case XVIII.—Male, aged fifty-six years. Died of Addison's disease. There is no distinct longitudinal muscular layer in the intima of the aorta. There is pronounced fatty degeneration of this tunic, particularly its deeper layer which is composed of coarse elastic fibers and connective tissue or muscular cells. Both of these elements are extensively degenerated, and the Sudan stain shows this fatty degeneration to extend to the muscular elements throughout about half the thickness of the media. There is considerable diffuse and perivascular round-cell infiltration in both these coats. Both renals show the elastica interna as well-defined elastic layers with only the slightest fission, these fissures containing a few connective or muscu-

lar cells. There is slight thickening in the connective tissue layer of the intima in two or three places in these vessels. The elastica interna of the splenic is split up into different layers or bundles. There is pronounced thickening of the connective-tissue elements of the intima involving about half the vessel's circumference. In the coronaries there are well-defined longitudinal muscular layers in the deeper portion of the intima, one of which extends throughout the entire circumference of the vessel and is enclosed between definite elastic lamellæ. This layer shows marked fatty degeneration, while the superficial or connective tissue layer is only very slightly involved. The basilar and præfossæ Sylvii show hyperplasia of their connective-tissue layer and slight fission of the elastica interna, the latter in the former vessel having taken the Sudan stain. It is uncertain if the small-cell infiltration seen in several of these vessels is a part of the Addison's disease, or secondary to the extensive fatty degeneration.

Case XIX.—Female, aged sixty years. Cause of death unknown. The larger vessels were markedly sclerotic. There is extensive fatty degeneration of the intima, most pronounced in the deeper layer, which is composed of coarse fibers and longitudinal muscle cells. There is a sparse diffusion of small cells in the intima. The media shows no degeneration. The renals and right vertebral show connective-tissue thickening and fission of the elastica interna. Extensive fatty degeneration of this coat of the latter vessel, particularly its deeper portion, is present, involving both cellular and elastic elements.

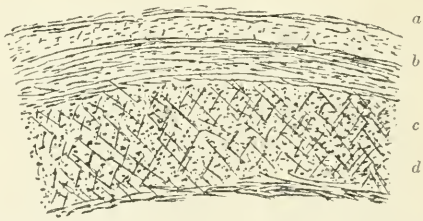

Fig. 5.—Longitudinal section of tertiary branch of the pulmonary artery in Case VI, a man, aged thirty-three years. *b* represents the longitudinal elastico-muscular layer of the intima, and *d* the elastica externa.

Case XX.—Male, aged seventy-six years. Died of influenza (?). There are plate-like sclerotic and atheromatous patches in the aorta. These show very little fatty degeneration, while the deeper layer of the intima shows large confluent fat masses, a few round cells, and beginning fibrous tissue formation. A fairly well-defined longitudinal elasticomuscular layer is seen. There is no fatty degeneration in the pulmonalis. Both renals show pronounced thickenings in the connective-tissue layer of the intima and some fission of the elastica interna, the latter as well as the contiguous portion of the

media shows slight fatty changes. The intima of the splenic is greatly thickened, its elastica interna split up into several layers and bundles of fibers, with inclusions of connective tissue or muscular cells. In the descending branch of the left coronary there is extensive fatty degeneration of the deep layer of the intima, which is composed of coarse longitudinal elastic fibers and longitudinal muscular cells. The superficial layer is greatly thickened, but not so extensively degenerated. The right coronary is very much the same. There is thickening of the intima in the præfossæ Sylvii, with fission and fibrillation of its elastic elements.

The average age of the above cases was thirty-seven years, the youngest being aged four months and the oldest seventy-six years. Fifteen were males and 5 females. Eight revealed some hypertrophy of the heart, but in only 2 was it at all pronounced. One of these was a case of chronic interstitial nephritis, and the other one of aortic insufficiency. Fourteen, aged on the average fifty-one years, revealed sclerosis or atheroma. The 9 cases which showed fatty spots on the intima were aged on the average thirty-five years, but one or two were infants. All of this latter group either died of infectious diseases or showed definite evidence of past infection, except one, which was a case of primary pulmonary sclerosis with the cause of death unknown. In a number the two conditions were combined.

Eliminating Cases V and VI, the former being syphilitic and the latter primary pulmonary sclerosis, it is worthy of note that no case of sclerosis or atheroma occurred below the thirty-eighth year of life. Considering that these cases were selected from about 300 autopsies, with a view of studying as early sclerotic changes as possible, the proof lies very near, that true sclerosis or atheroma is invariably the expression of involutional or senile changes.

This agrees well with the age at which other senile changes begin to appear, notably, asbestos-like degeneration of the costal cartilages, which is generally recognized as one of the earliest histological manifestations of senility.

Excepting the superficial fatty spots, the changes which I have described as occurring in the intima, before this period of life, are in every sense physiological, and consist chiefly in the thickening of the elastic and muscular elements in the deeper layer of the intima, notably in the aorta, but also to a considerable extent in the other vessels. The slight fissions and lamellations of the elastica interna, with the development of connective or muscular tissue in the intervening spaces, are no wise to be considered the expression of sclerotic changes. They have undoubtedly often been taken for such.

The age at which the physiological development of the vessels is completed varies somewhat with the individual and the vessels concerned. Jores and his pupils, and H. Voigt have worked this out

for the aorta, Smiedel for the mesenteric, and Hallenberger for the radials. Thayer and Fabyan have also shown the gradual thickening of the latter vessel with advancing age.

Ashoff declares that longitudinal muscular bands or layers do not occur in the intima of the smaller vessels except near their point of bifurcation. This is by no menas always the case.

While the results of my studies confirm, in the main, those of Voigt as to the splitting up of the elastica interna of the aorta into two elastic lamellæ and the subsequent laying down of the deeper elasticomuscular layer and a hyperplastic middle layer, I have found that the process does not always proceed with such regularity as his work would suggest.

Younger cases sometimes show the development more pronouncedly than older ones, and occasionally the three definite coats of the intima cannot be made out.

There has been nothing in my cases to suggest that the media plays any part or is in any way altered in the beginning of atherosclerosis. After the process is once well established, hypertrophy of the media occurs, and may, when later impinged upon by the thickened intima, degenerate. The first demonstrable alteration has usually been a thickening of the connective-tissue layer of the intima, and to this, if the condition advances sufficiently, is subsequently added fatty degeneration of the connective-tissue cells, muscular elements, and elastic fibers of the deeper layer of the intima.

The condition is, therefore, primarily hyperplastic, secondarily degenerative, but in no wise inflammatory. I cannot, therefore, agree with Jores that fatty degeneration is the *sine qua non* of sclerosis of the senile type.

If the experiments of Durant, on the effect upon the intima of the destruction of the vasi vasorum and the injection of the lymph channels, as well as those of Bubnoff and Köster on the transportation of cinnabar granules from the surface of the adventitia to the lumen of a ligated segment of a vessel, required further proof of the nutritional dependence of the intima upon the circulation in the vessel wall, the demonstration of capillaries in the intima and the immediately contiguous portion of the media, in Cases II and IV, would certainly be convincing.

In this connection the following recent statement of Adami is somewhat surprising. He says: "The intima is non-vascular, it receives its nourishment by diffusion from the plasma within the aorta, as, indeed, would seem to be the case with the inner layer of the media."

The small cell infiltrations which have occasionally been observed, in and about the fatty spots of the intima have undoubtedly reached their location by means of the lymph and blood circulating in the vessel wall, or else have proliferated, *in situ*, from already existing

cells, and not, as Traub supposed, by a deposition from the blood stream.

Conclusions. 1. While the elastica interna of most of the vessels at birth consists of a definite single lamella, this is capable of undergoing subsequent fission into two or more lamellæ during the developmental period of life.

Within the first year of life the elastica interna of the aorta shows two definite parallel, closely lying lamellæ, between which a narrow, longitudinal muscular layer has appeared. This latter undergoes a gradual thickening, within which appears a considerable number of rather coarse elastic fibers. The deeper lamella of the two remains throughout life as a distinct limiting layer between the longitudinal elasticomuscular layer and the media. The inner or more superficial one gradually breaks up into a coarse, firm, elastic latticework, enclosing in its meshes a few muscular and connective-tissue cells, which probably are the active factors in the breaking up of this lamella.

The connective tissue, or lumenal layer of the intima, becomes slightly better developed and contains, especially along its lumenal border, a very fine meshwork of delicate elastic fibrillæ.

In such vessels as the iliacs, subclavian, celiac, and sometimes the renals, radial, splenic, and coronaries, fission of the elastica interna, with the deposition of a longitudinal muscular layer or bands, is frequently observed by the fortieth year of life. The time at which this appears varies with the individual and the vessels concerned. It is not always present. They have no doubt frequently been mistaken for sclerotic processes.

2. It is reasonably certain that many of the cells observed in the fissures and clefts of the elastica interna, in the smaller vessels, are muscle cells and occupy an analogous position to the longitudinal muscular layer of the aorta.

3. The fatty spots so commonly observed on the intima bear no actual or causal relation to atherosclerosis. They invariably begin in the superficial layer of the intima and are usually a manifestation of infection.

4. The type of sclerosis here considered is invariably the expression of senility, and very rarely occurs before the fifth decade of life. Its earliest manifestations begin, invariably, in the intima, and are characterized by a hyperplasia of its connective-tissue layer and also its deeper elasticomuscular layer, the latter subsequently undergoing degeneration of both its cellular and elastic elements. It is impossible to say whether the fatty degeneration of the elastic fibers begins in the fibers themselves or in their cement substance.

5. The primary causes of atherosclerosis is an exhaustion of the elasticity of the elastic tissue in the vessel wall, and the hyperplastic changes in the intima are compensatory.

There is no histological evidence of a primary involvement of

any elements in the media, and a fatty degeneration of the elastic fibers of this tunic is very rarely seen.

6. No one has been able to produce atherosclerosis experimentally.

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REVIEWS

Dyspepsia: Its Varieties and Treatment. By W. Soltau Fenwick, M.D., Doctor of Medicine of the University of Strassburg; Late Physician to the Evelina Hospital for Sick Children, etc. Pp. 485; 10 illustrations. Philadelphia and London: W. B. Saunders Company, 1910.

This work is a compilation to a less degree than almost any other work on gastro-intestinal conditions, but rather presents the results of the author's investigations and clinical experience. One commendable feature is the definite statement of the frequency of various symptoms as determined by careful statistical studies of large series of cases. It is to be noted with appreciation that Dr. Fenwick harbors no illusions regarding the accuracy of these statistics. Indeed, in several places he calls attention to the fact that some of the statistics, if gathered in another way, as, for example, in private instead of hospital practice, actually do or probably would show very different results. But at least such statistics provide a starting point that is definite and can only be modified or corrected by further and more careful studies of a similar nature. Once they are published they do away for all time with beliefs, impressions, or opinions. Dr. Cabot has recently laid particular emphasis upon this point.

The book itself is a monograph rather than a text-book. The subject is thoroughly covered, and the reviewer must confess to a slight feeling of surprise when he found included a long section on the chronic gastro-enteritis of infancy. There is, however, no reason, either anatomical, physiological, or pathological, why diseases of the gastro-intestinal tract of infants should be separated from those of adults. On the other hand, the dyspepsias due to ulcer and cancer of the stomach are not discussed, for the excellent reason that the author has considered them elsewhere.

Indigestion is classified into gastric, of which eight types are recognized, and intestinal. This is followed by a tabulation of 1000 cases, and a brief classification of symptoms which constitutes, in a way, a key to diagnosis.

One of the most interesting chapters is that entitled myasthenia gastrica. Dr. Fenwick believes implicitly in the existence of a motor insufficiency and retention without obstruction. There are

interesting tabulations of the age incidence, which, from the difficulty of determining the time of onset of insidious chronic disorders, are not particularly convincing.

The displacements of the stomach are divided into upward, vertical, and total descent. The distinction between the last two is difficult to make.

The chapter on dyspepsia due to the presence of foreign bodies or living creatures in the stomach contains a large amount of curious information.

The section on the chronic gastro-enteritis of infancy is one of the most admirable in the book. Dr. Fenwick believes that even should infants recover, permanent lesions of the gastro-intestinal tract remain in many cases, and his personal studies seem strongly to support this contention.

Only one-tenth of the book is devoted to intestinal indigestion, which is divided into chronic intestinal indigestion, chronic pancreatitis, duodenitis, and enterospasm. Just why the dyspepsia due to chronic pancreatitis should be regarded as an independent form and that due to disease of the liver as secondary is not entirely clear.

One hesitates, however, to find any fault with this book. The subject is so admirably presented, the method of presentation is so original and thorough, that it must be regarded as a valuable contribution to the disorders of digestion. The paragraphs on treatment present very little that is new. Indeed, it may be said that gastro-enterologists agree fairly well regarding therapeutic measures. Three points regarding the arrangement of the book may be noticed. The literary references are conveniently collected at the end and the reader's attention is not distracted by figures in the text. There is, however, no difficulty in discovering any reference that may be desired. The illustrations are few. Each one is apparently carefully selected for a definite purpose. The book is delightfully light, actually weighing just two pounds, which is considerably less than the average of medical books of the same size. J. S.

Dawn of the Fourth Era in Surgery. By Robert T. Morris, A.M., M.D., Professor of Surgery in the New York Post-Graduate Medical School and Hospital. Pp. 145; 6 illustrations. Philadelphia and London: W. B. Saunders Company, 1910.

This collection of reprints from the pen of a ready writer, whose heart always is inditing of a good matter, is a welcome addition to the surgeon's library shelf. They are republished as originally printed, except that "here and there a word has been added for

the same reason that one drops an egg into a pot of coffee, and because of Mark Twain's discovery that the difference between the right word and almost the right word is the difference between lightning and the lightning-bug."

Dr. Morris is nothing if not an extremist, but while he may make us laugh and carry us along with him in some absurd argument to the end of an article, it is rarely difficult, on sober second thought, to detect the fallacy in his reasoning. The usual fallacy is that of the "heap of stones." One is asked if 100 stones make a a heap of stones, and he replies yes; but if we remove 1, will 99 stones still be a heap? Yes, to be sure. And so we go on down the scale, until finally, when the question is asked if 3 stones lying together make a heap, the victim rebels, and says, No, they don't! To this we reply: But you acknowledged that 23 stones, 22 stones, even 18, 17, 16, and 10 stones made a heap; that 9, 8, 7, 6, 5, and 4 stones still made a heap; but when 3 stones alone are left, you say it is no longer a heap—how is that? Of course, as we abstract stone by stone from the heap it must some time cease to be a heap; and Dr. Morris's one failing seems to be an inability to see as soon as others that his "heap" of stones is degenerating into "one or two stones."

In the "Hand of Iron in the Glove of Rubber," "Gall Spider Cases," and "Back to an Old Idea" this tendency is preëminently manifest. But all the papers are interesting, instructive, and well worth the little time it takes to read them, and the longer time required to think them over after they have been read.

A. P. C. A.

INNERE SEKRETION. IHRE PHYSIOLOGISCHEN GRUNDLAGEN UND IHRE BEDEUTUNG FÜR DIE PATHOLOGIE. By PROF. DR. ARTUR BIEDL. Mit einem Vorwort von HOFRAT PROF. DR. R. PALTAUF. Pp. 538. Berlin and Vienna: Urban and Schwarzenberg, 1910.

THIS book, essentially a monographic enlargement of a previously published compendium by the author, presents the collected material in the usual thoroughgoing fashion of the German writers. The work has the distinction, however, of being in the hands of an able investigator, a man of wide experience, a master not only of the literature, but also in command of a splendid first-hand knowledge of the objective side of his subject. The introductory pages by Paltauf fail, however, to give the reader the proper impression of the character of the work, and are in no sense so noteworthy as might be expected from a man of his literary and scientific attainment.

The book itself is divided into two parts. The first part takes

up the general phases of internal secretion, the history, limitations, and definitions, the various forms of hormones, their method of action, their origin, the sources of our knowledge concerning them, and the experimental procedures availed of in gaining our present knowledge of the subject.

The second part, with utmost catholicity, takes up the embryology, anatomy, physiology, and pathology of the various organs and systems of organs concerned in internal secretion. The thyroid (and parathyroid), thymus, adrenal system (chromaffin system), hypothesis, pineal body, and sexual glands are considered in extenso. The pancreas, gastro-intestinal mucosa, and the kidney are considered somewhat less fully, but nevertheless, in a very satisfying manner. This much of the book takes up 407 pages and is followed by an extensive presentation of the literature, occupying 129 pages in small type.

Throughout the book the facts at hand are given precise and careful attention, are presented logically, and with due attention to the methods of demonstration. The writer keeps clearly in mind the difference between proved and unproved, and while not permitting himself to indulge in verbose and vain speculation, yet allows his imagination free play where hypothesis has definite foundation in established fact. The ultimate application of the facts and hypotheses to man is ever prominent, the author giving this phase of the subject most careful attention.

Embryology and anatomy gain little from this book. Physiology profits much by the masterful presentation in compact form of the facts gleaned from wide and diverse sources. Dynamic pathology, however, is given a tremendous impetus by the work, for not only is the pathologist given a broad view of the subject in general, but the book is brimming with suggestion of the application of this sort of physiology to pathological processes, and the thoughtful reader with a mind awake to the vast possibilities of this field of work cannot fail to be stimulated to new endeavor in the search for truth.

The writer gives much due credit to American workers for their share in the development of our knowledge of internal secretions, but unfortunately has been unable to present some of the facts more recently developed in America, a feature too well known in Continental books to need more than passing comment and lasting regret.

The book is printed in large, clean type on smooth, heavy paper, the subject matter being carefully arranged, well paragraphed, and important points usually, but not constantly, printed in heavy-faced type. The work as a whole is of such a high order of merit as to deserve most careful and thoughtful perusal by both clinician and laboratory worker. H. T. K.

PUBLIC HYGIENE. By THOMAS S. BLAIR, M.D. Assisted by numerous contributors. In two volumes; pp. 953; numerous illustrations. Boston: Richard B. Badger, 1911.

DIFFERENT chapters are written wholly or in part by sixteen contributors; the remaining nine chapters, as well as the material added to the chapters contributed by others, are written by Dr. Blair. Besides the collaborators, a number of individuals and organizations are mentioned that have supplied data, reprints, photographs, etc.

The book is divided into twenty-five chapters, as follows: The family versus the community; hotels, lodging houses, and public buildings; school inspection and college sanitation; penal institutions and hospitals for the insane; maternities; places of amusement and dissipation; slums and town nuisances; special rural hygiene and sanitation; state departments and boards of health; a proposed federal bureau of health; local boards of health, county and sanitary officers; army and navy sanitation and hygiene of camps; the coroner and the physician; quarantine; infectious diseases; immunity; epidemics; disinfection; tuberculosis sanitaria and dispensaries; home hygiene and interior sanitary installation and gas installation; pure drugs and foods; public works and corporations; public carriers and sanitation; laboratory methods in sanitation; medical societies and sanitation. In an appendix is given a brief summary of the infectious diseases of animals communicable to man, along with several other matters of minor importance.

The two volumes consist of 953 pages, with numerous half- and full-page photographic illustrations, many of which can convey very little information concerning the public health, and appear to be introduced largely to swell the size of the book and to increase its cost.

Judging from the preface, the editor aims to administer a rebuke to those intrusted with the administration of sanitary affairs and to laboratory men, because, he states, "the decision has been reached that public hygiene has developed too much as a specialty and needs the temperate conclusions of the whole body of the medical profession. Such conclusions must result from a careful comparison of laboratory and clinical data, and no one class of men are so fully qualified to weigh them as is the class to whom this volume is especially addressed.

"But in order to so, the family doctor must inform himself, not only upon the pathological and clinical aspects of the work, but also upon the sociological, legal, and engineering factors involved. The effort is here made to present reliable data upon the present very creditable development of this important subject and, in doing so, the author poses more as an editor than as an original writer, and has endeavored to judicially weigh the evidence at

hand upon a basis of real accomplishment, rather than that of a propaganda."

Altogether the work is a great disappointment in that it fails to give information on important phases of the subject that might be elucidated, and the matter that is given is presented in such a haphazard and jumbled way as to make it altogether unsatisfactory.

D. H. B.

Introduction to Vertebrate Embryology. By Albert Moore Reese, Professor of Zoölogy in West Virginia University. Second edition, revised and enlarged; pp. 340; 118 illustrations. New York and London: G. P. Putnam's Sons, 1909.

The book contains a direct and concise account of the more general features of the development of the frog and chick, together with a chapter on mammalian embryology. As the author states in his preface, it is a compilation into convenient form of only the important facts, and is especially suited for those wishing an introduction to the subject. The illustrations are, for the most part, selected from larger and more comprehensive works, and serve as useful adjuncts to the text. In this second edition the enlargement consists of the addition of a chapter of 45 pages on mammalian development, which makes the book more useful, especially for premedical students.

Although no directions are given for laboratory work, it is understood that this is to accompany the study of the text. Indeed, it is only with careful laboratory work that full educational value can be derived from the study of embryology. The study of serial sections of entire embryos is especially valuable in giving the student a plastic imagination.

In following the continuous changes which are occurring during development, it is possible to select only certain well-marked stages for description, but these must be described fully enough to be plainly understood. In such a subject as embryology it is especially true that brevity is not always compatible with clearness. The author has apparently succeeded in choosing the middle path, and with the aid of the illustrations presents a lucid account of his subject.

In the descriptions of the figures, no magnification is given, with the view, perhaps, of not adding a detail which would be useless or confusing. It is probable, however, that the lack of this information often causes considerable uncertainty in the student's mind, and may be even misleading, especially as in the present case where the figures come from diverse sources.

The fact that a second edition has been called for shows that the book has been found useful, and is also a hopeful sign that the value of the study of embryology is being appreciated. W. H. F. A.

CHEMISTRY OF FOOD AND NUTRITION, By HENRY C. SHERMAN, Ph.D., Professor in Columbia College. Pp. 355. New York: The Macmillan Company, 1911.

THE number of books pertaining to the chemistry of foodstuffs is legion, and it would seem that with library shelves groaning under the weight of treatises on food and nutrition, the *furor scribendi*, which is epidemic at present, should be held somewhat in check. In a way these multitudinous books have a purpose quite apart from their table of contents. They are blazing a trail through a subject which, in America, at any rate, has been woefully ignored, and are atracting attention to a field of science which is so near to medicine that it has been overlooked by the hyperopic vision of most physicians. This purpose is commendable, but it may be defeated by the almost infinite number of books devoted to this study, since the searcher for knowledge of the subject stands aghast at the outset of his quest by the rows upon rows of imposing volumes. In his dismay he feels that to choose one work from so many is beyond his ken, and flees the task.

The book under review is a concise, well-written, and extremely accurate exposition of the subject with which it deals. The chemistry of foods themselves is contained in a rather short chapter, but broad enough in scope to give a clear idea of general principles. The remainder of the work is devoted to food in its nutritive relations, that is, the action of ferments, the course of the food through the digestive tract and its fate, the food requirements of the body, both organic and inorganic, with a complete table of the protein, fat and carbohydrate content of foods and their fuel value. The book comprises only about 350 pages, but in these the author has given more than a glimpse of the subject, and offers his reading matter in a well-prepared, easily, and pleasantly assimilable form.

E. H. G.

A MANUAL OF PHYSICAL DIAGNOSIS. By BRESNEY R. O'REILLY, M.D., C.M., Demonstrator in Clinical Medicine and Pathology, University of Toronto; Assistant Physician to St. Michael's Hospital, Toronto. Pp. 369; 6 plates and 49 illustrations. Philadelphia: P. Blakiston's Son & Co., 1911.

THE author of this epitome of physical diagnosis has brought out a book which should be of especial value to the student. He deals with his subject in a thorough and careful manner. His explanations and descriptions, while concise and brief, are yet so clear that they can be readily understood by the beginner in the study of this subject. The book will also prove useful to the prac-

titioner and teacher. Many of the signs of physical diagnosis, named after the original describer, are easily forgotten and with difficulty sought out, here may be found the complete summary of of all these signs, easy to reach and to rapidly review.

A few criticisms of the author's style and handling of his subject matter may be made. There is a splendid epitome of the polygraph with complete interpretations of the graphic tracings produced, but unfortunately, the author has seen fit to dismiss sphygmomanometry with but a few lines. The addition of the appendix seems to be unnecessary. Clinical laboratory methods are much better left to the larger works on this subject. In the explanations of the methods of laboratory procedure, there is a tendency to be too brief, so that they are of little value except for the seasoned laboratory man. As an example of excessive brevity, we find no mention of the use of glacial acetic acid in the benzidine test for occult blood.

While a few other minor criticisms might be made, in its entirety the book is a clean cut, complete exposition of an important subject. J. H. M., Jr.

Manual of Cystoscopy. By J. Bentley Squier, M.D., Professor of Genito-urinary Surgery, New York Post-Graduate Medical School and Hospital and Henry G. Bugbee, M.D., Instructor in Genito-urinary Surgery, New York Post-Graduate Medical School and Hospital. Pp. 117; 26 illustrations. New York: Paul B. Hoeber, 1911.

This small volume has been prepared to meet the demands of students for a short, practical work on cystoscopy. With this object in view, the authors have eliminated detail, confining themselves to a concise but clear description of cystoscopic technique, normal as well as pathological bladder pictures and ureteral catheterization. The illustrations are unusually well executed and in several instances schemtatic drawings are included to further elucidate the colored plates. The book can be highly recommended to the beginner in this line of work. F. E. K.

Radium. Its Physics and Therapeutics. By Dawson Turner, B.A., M.D., F.R.C.P., (Edin.) M.R.C.P. (Lond.), F.R.S. (Edin.), Lecturer on Medical Physics, Surgeons' Hall, Edinburgh, etc. Pp. 86; 27 illustrations. New York: William Wood & Co., 1911.

The author's objects in presenting this publication are: (1) To give, in a concise form, to those of the medical profession inter-

ested in the subject, but unfamiliar with it, a brief outline of the discoveries, investigations, and published works of physicists of the highest recognized authority along the line of radioactivity. (2) To explain briefly the physiologic action, therapeutic effects, and therapeutic applications of radium, and the methods of employing it as a therapeutic agent. (3) To show the results in general that have followed its use, and the results of the author's own experience in radiotherapy during a period of five years. This book would be found especially valuable to anyone unfamiliar with the subject who might wish to obtain a general idea of any part or all of it in a comparatively short time. H. K. P.

Gynecological Therapeutics. By S. Jervois Aarons, M.D. (Edin.), M.R.C.P. (Lond.), Gynecologist to St. Anthony's Hospital; Fellow of the Royal Society of Medicine, Member of Obstetric and Gynecologic Sections; Formerly Registrar and Pathologist to the Hospital for Women, Soho Square; Gynecological Tutor, Extra-mural School of Medicine, Edinburgh; House-surgeon, Gynecological Ward, Royal Infirmary, Edinburgh. With foreword by Sir Halliday Croom, M.D., F.R.C.P., F.R.C.S., Professor of Midwifery in the University of Edinburgh. Pp. 178; 43 illustrations. New York: William Wood & Co., 1910.

This book of 178 pages deals solely with the medical treatment of gynecological affections. The author has taken up the various lesions in a systematic manner, and briefly but clearly outlines measures which his own experience has proved of value. Numerous prescriptions are included as well as definite instructions concerning local applications and the use of pessaries. The book presents a comprehensive review of modern gynecological therapeutics and will be of distinct service to the general practitioner for whom it is intended. F. E. K.

Vicious Circles in Disease. By Jamieson B. Henry, M.A., M.D., Ex-President, Reading Pathological Society. Pp. 186; 10 pages illustrative diagrams. Philadelphia: P. Blakiston's Son & Co., 1911.

This little monograph is a distinctly novel and interesting contribution to medical literature, and one is at once impressed by

the large number of vicious circles the author is able to cite, to the authenticity of which most readers can testify from their own experience. From the publishers' standpoint, the book is attractively bound in cloth, printed on heavy paper and in large type, this feature being especially commended.

After a short introduction, in which the important part that vicious circles play in pathology is sufficiently emphasized, the author divides his subject matter into twelve chapters, dealing respectively with the classification of circles, which he divides into organic, mechanical, infective, neurotic, etc., circles associated with the nervous system, and in order, circles associated with the cardiovascular system, the respiratory system, the digestive system, the urinary system, the sexual system, with the eyes and eyelids. Then folllows an interesting chapter devoted to artificial circles, not caused by, but leading to disease, such as excessive purgation, excessive abuse of alcohol, tobacco, morphine, the use of strychnine in shock, the use of restraint in the case of the insane, etc. Next a chapter entitled The Genesis of the Circle, in which is discussed various pathological conditions giving rise to circles; then a chapter devoted to the discussion of the breaking of the circle, first by natural means, and secondly by treatment, in the latter case emphasizing the importance of breaking the circle at its weakest point and finally the author states his conclusions.

The one criticism advanced, if criticism it be, lies in the rather too frequent use of Greek, Latin, and French quotations and ex-extracts to illustrate and reënforce the author's meaning.

V. L.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Gastric Analysis.—Benton and Tidy (*Quart. Jour. Med.*, 1911, iv, 449) studied 331 test meals of toast and tea at the London Hospital. In cases of gastric carcinoma Günsberg's reagent gave a negative test and the total acidity was highest when the lesion was at the pyloric end. With a low acidity, it was either in the cardia or in the body of the stomach and inoperable. Taken in connection with the length of history given by the patient, the gastric analysis is of some importance. A patient with carcinoma and a gastric history of less than two years almost certainly has no free HCl in the test meal. One with a gastric history of more than four years and no free HCl almost certainly has no carcinoma. In the rare cases of carcinoma grafted on an old ulcer there was generally presence of free HCl and the total acidity was normal or above. Thus, the picture resembles the ulcer type. In the cases of ulcer it was observed that marked anemia may lead to a diminution of the free HCl. Especially is this the case after severe hemorrhage. And it is noteworthy that free hemorrhage may lead to an amelioration of the symptoms. Dyspeptic cases with low acidity early lost their symptoms on the administration of acids. This furnished a good clinical differentiation from carcinoma, where the acidity is usually unchanged and the symptoms unmodified. In dealing with free acidity they found Günsberg's reagent of much greater importance than the dimethylamidoazobenzene. The methods generally in use are approximately accurate when the free acidity is normal or above normal, and not so accurate when it is below, while the phosphates which are secreted into the stomach when the mucous membrane fails

to elaborate HCl detract from the accuracy of ordinary methods. This inaccuracy is common to all methods. Therefore, the simple Günsberg reaction with estimation of dimethyl acidity and total acidity by phenolphthalein are quite sufficient.

Cultivation of Treponema Pallidum.—While several investigators have produced a spirochete morphologically the pallidum, this parasite has never yet been grown to reproduce syphilitic lesions. Noguchi (*Jour. Amer. Med. Assoc.*, 1911, lvii, 102) using the testicular tissue of rabbits, grew the treponema upon serum water to which sterile rabbit kidney or liver had been added. At first strict anaërobic conditions are necessary. As the cultures contained bacteria too, Noguchi was able to effect purification by letting them grow through a Berkefeld filter, which held back the bacteria. Later they may be recovered from the bacteria from stab cultures in solid media. Their pathogenicity for rabbits has been proved, and the same lesions are found as in those set up by inoculation with luetic material. This establishes the fact that the treponema is the cause of the lesions in man.

Effects upon Complement Fixation Test of Arsenobenzol.—Craig (*Arch. Int. Med.*, 1911, viii, 395) has studied 225 cases out of over 700 at his disposal. The histories of these selected men were full as to date of infection, stage of the disease, and immediate results of treatment. The best results of treatment are with cases in the primary stage of the disease—the worst with tertiary manifestations—but the complement fixation test disappears more rapidly in the tertiary stage cases. The explanation of this is that a positive test means the presence of living spirochetes, and whereas in the primary stage there were a large number of spirochetes in the patient, in almost all tertiary cases the patient had had courses of mercury and the organisms were readily killed off. This observation of the rapid disappearance of the complement fixation test in the tertiary stage coincides with the clinical observations where one observes rapid healing of tertiaries following salvarsan. In most cases the reaction disappeared in the second, third, and fourth weeks of treatment. The prognosis is most favorable with those cases showing a weak fixation, and least favorable with the cases showing a strong (100 per cent.) fixation. They tried very few cases with the intravenous method. Alkaline suspensions were better than neutral when used intramuscularly, and the reaction disappeared faster after intravenous than intramuscular injection. While the time of disappearance of the reaction was little affected, better results were obtained in those cases who had mercurial treatment. One or two injections of "606" seemed more efficacious than two years of mercury. The reaction furnishes the only test of whether lues is cured or not, and one must wait a reasonable time to get the reaction.

The Physiology of Passive Movements.—Veiel and Zahn (*Münch. med. Woch.*, 1911, lviii, 1759). While passive movement has been used for some time in the therapy of cardiac disease, there has been as yet no accurate observation of the exact effects upon the system.

Recently Veiel and Zahn have been able to conduct such experiments in Romberg's clinic with Büdingen's apparatus. This consists of an electrically driven machine, by means of which the legs of patients can be put through the motions of ordinary walking and hill climbing. Two arms are operated by the mechanism, to each of which a leg is fastened. The speed and length of stride can be altered at will. They found that these passive movements produced a greater flow of blood in the legs, the flow in the arms being less in compensation. The striking force of the heart is greater. The circulation is influenced in the same way, but in a milder degree than in active movements. There is no general rise in blood pressure as is seen in active movements, and the heart acceleration is absent. The exercises are particularly useful in bedridden patients, preventing marantic thrombi because of blood stasis. They are particularly indicated in cases of mild or medium grades of cardiac insufficiency, where it is essential to improve the peripheral circulation, and at the same time give mild exercise to the heart. The exercises are of the same sphere of usefulness as CO_2 baths and massage.

The Excretion of Uric Acid by the Kidney.—Frank and Bauch (*Berlin. klin. Woch.*, 1911, xlviii, 1463) investigated clinically the effect of atophon (2 phenylchinolin, 4 carbon acid, supposed to be a remedy for gout) on the excretion of uric acid. The patients were on purin free diet and were of the gouty diatheses. Uric acid given intravenously was always followed by a more considerable output of uric acid if atophon had also been administered. It is very probable that atophon changed over the uric acid into an easily soluble component. From their observations they conclude that the teaching of an interrupted or more difficult uric acid excretion is not far wrong as a cause of gout. They feel that Brugsch and Schillenhelm's hypothesis, that the uricolytic ferments are at fault, is wrong, because when one can recover almost quantitatively uric acid introduced intravenously, there would not be time for these ferments to work. It is more probable that gout depends on a difficult excretion of uric acid by the kidneys. But it is improbable that this is part and parcel of either an anatomical function or a renal insufficiency. It is probable that the difficulty in excretion depends on a definite decrease in individual cell power, some cells being especially reserved for the excretion of each urinary component. Most, but not all of the uric acid is excreted by the tubuli contorti. As these cells are damaged this selective action disappears and the acid is excreted from other parts of the kidney. Atophon has seemed the key to raise the damaged cells to their old stage of usefulness.

Salvarsan in Late Lues of the Nervous System.—Assman (*Deut. med. Woch.*, 1911, xxxvii, 1603) has investigated 8 cases of general paralysis with 6 of tabes dorsalis and several of syphilitic nervous system diseases. The "606" was given in various ways, sometimes intramuscularly, but generally intravenously, in small, repeated doses. In six weeks' observation on paralysis of the insane there was a general improvement of the condition either observable clinically or by the

Wassermann reaction or by the character of the spinal fluid. In some cases of tabes there was improvement of the lancinating pains and gastric crises, but never an improvement of the objective nervous phenomena. Generally there was slight change in the character of the cerebrospinal fluid lymphocytosis (Nonnes reaction), but in 2 cases this improvement was very marked. The Wassermann reaction in the blood and spinal fluid was not influenced. In lues of the cerebrospinal system not only the clinical symptoms but also the cerebrospinal fluid was much improved in all its characters.

The Nitrogen and Chloride Excretion by the Skin.—Loofs (*Deut. Arch. f. klin. Med.*, 1911, ciii, 563). The amount of nitrogen and chloride excreted by the skin is interesting, for in cases of renal insufficiency all authorities from von Ziemsen have advocated improving elimination by vigorous stimulation of the skin and bowels. Loofs studied the amount of nitrogen and chloride excreted into clean absorbent towels by patients in various stages of nephritis. Three cases of tuberculosis were used as controls. In no case was there any increase in the amount of nitrogen or chloride excreted by the skin of nephritic patients, even in 2 cases where well-defined uremic symptoms were present. About 0.25 gram nitrogen and 0.2 gram sodium chloride were excreted in twenty-four hours. In 1 case of acute hemorrhagic nephritis the sodium chloride output was about doubled, but this patient was just recovering from edema.

Spectroscopy in Fecal Examination.—Csepai (*Deut. Arch. f. klin. Med.*, 1911, ciii, 459) compares the relative accuracy of investigation of feces and gastric contents for blood. He finds that the most sensitive test is the benzidin, which depends on the catalytic action of benzidin and hydrogen peroxide. The old crystallization of hematin tests have been abandoned because of their lack of sensitiveness. The catalysis tests are not as good as one could wish, because they react to plant chlorophyll and other bodies and because the reagent readily spoils. He recommends a spectroscopic test. The instrument used may be of the cheapest variety; 5 c.c. each of concentrated acetic acid, alcohol, and ether are rubbed up for a few minutes into about 5 grams of feces, then filtered through a dry paper. To this extract in a test-tube 1 to 2 c.c. of pyridin and 1 to 3 drops of ammonium sulphide are added. The resulting mixture in the presence of blood shows the spectrum of hemochromogen. The patient should, of course, be on a hemoglobin and chlorophyl free diet for about three days before the test, *i. e.*, he should have no meat or green vegetables. The test must be done immediately after the addition of the ammonium sulphide, for delay causes weakening of the absorption spectrum.

The Action of the Vagus on the Human Heart.—Robinson and Draper (*Jour. Exper. Med.*, 1911, xiv, 217). While it has been possible to show the accurate effects of mechanical vagus stimulation upon the heart of lower animals, it is only recently with the aid of the electrocardiograph that it has been possible to do this in man. In a normal man, Robinson and Draper produced slowing of both auricles

and ventricles and delay in the A-C time, and probably the left ventricle was diminished in force of contraction. Stimulation of the right vagus has more effect on the heart rate and force of ventricular contraction than the left, but the left has more influence on the conductivity from auricle to ventricle. Right-sided stimulation increased the action current of the ventricles, *i. e.*, there was a bigger "R" wave, while the left vagus produced an opposite effect. There was no difference in the current of auricular contraction, nor were any changes in excitability of auricle or ventricle produced. In cases of auricular fibrillation, stimulation of the right vagus caused slowing or stopping of the ventricular rhythm with no effect upon the electrocardiographic register of the auricular fibrillation. While the effect of vagus stimulation on fibrillating auricles in animals is still unsettled, it is probable that it is an apparent arrest and is in reality due to the powerful depression of the force of auricular contraction. No one would venture to so powerfully stimulate the vagus in man in the light of Quincke's advice. In all probability these pauses might be due to blocking of the auricular stimuli. After vagus stimulation the force of ventricular systole is much weakened for several beats. The excitability of the ventricles may be lowered, although there is no change in the auricles.

Animal Experiments in Goitre.—Gouget (*Presse Médical*, 1911, 709). The idea that the endemic development of goitre is due to the water drunk is not new, and always has been favorably received. Goitre is seen in the endemic districts in most domestic animals, of which the dog and rat are the most sensitive. Of 8 rats, 6 had pronounced goitre after drinking water when put in a Swiss goitrous district. The other 2 were young and escaped, for generally the malady attacks only adults. In the control animals who drank other waters but were housed and fed the same, there were no cases. In the test animals 50 per cent. of the young were stillborn and many others died early in life. Simple Berkefeld filtration does not protect the animal. Hence the exciting cause may be an ultramicroscopic organism or a soluble toxin. The filter was kept in milk and the milk given for over a year off the filter. There was no case of goitre among the animals, but a definite cretinoid state. Gouget finished by producing less marked goitres by the filtrates. All the goitrous animals had big hearts, not, he thought, due to the goitre, but both from one cause. Heating water apparently destroyed the causative agent. This agent was apparently derived from rocks over which the water ran, not only because of the richness of the water in lime salts, magnesium, and iodine contents, but also because of other properties. Gouget accordingly left ineffective water in contact with rocks from the streams of the goitrous areas. None of the animals using this water developed goitre except after long periods. Contrarily, he put struma-producing water in contact with jurassic rocks, and no goitre was produced in the animals taking it. It thus appeared that the goitrous toxin was fixed by some rocks, *i. e.*, the rocks lose their efficacy just like the filter. The presence of colloid in goitre led him to try dialysis. The dialyzed portion gave no goitre to animals. The water remaining in the dialyzer produced it readily. By the stalagmometer he found differences in surface ten-

sion of the dialyzed and remaining fluid, *i. e.*, the substance is colloidal. This harmonizes well with the lack of stability in transportation and heating. Repin has discovered that heat does not destroy the agent and that the diminution in struma producing qualities is proportional to the precipitation of the calcium salts; others that it is proportional to the poverty of the iodine salts. Beratch and Lesieur are accordingly precipitating iodine salts and observing results. These surely look hopeful.

Acid Intoxication in Diabetic Coma and other Diseases.—Porges (*Wien. klin. Woch.*, 1911, xxiv, 1147) reviews the various acids in coma diabeticum as well as the various forms and causes of other intoxications. The poisoning may be due to over accumulation of acids, to a deficiency of alkalies, or to an insufficient output of acids to which the condition is due. Acidosis is much more common than is generally supposed. It is characterized invariably by increased breathing and this may be a greater intake of breath at each respiration —hyperpnea—or an increase of the respiration. Lately it has become known that the respiratory centre is particularly sensitive to acids, and that the respiration is a means of throwing off the excess of acid in the blood. This acid is mainly carbonic acid. On finding a patient in coma where no history can be obtained, with nothing to explain the coma on physical examination, hyperpnea denotes that the condition is one of acid intoxication. In this condition, alkalies are indicated. On the contrary, the absence of excessive action of the lungs serves to exclude acidosis from diabetes or other cause. Meat and other proteins should in such a case be excluded from the diet. While they do not actually cause acidosis, they surely tend to increase it, and should be kept down in cases of nephritis and diabetes that show any tendency to become comatose. But under ordinary circumstances the organism is able to dispose of the acid elements of meat. Balint (*Berlin. klin. Woch.*, 1911, xlviii, 1580) advises the administration of sugar solution per rectum in those cases due to diabetes. The absorption is better and longer. By mouth the patient receives only 500 c.c. of bouillon, but this in addition to the 100 or 200 grams of sugar in the infusion gives him 700 to 800 calories per diem. Under this treatment the acid intoxication was materially reduced or even disappeared, and the reduction was proportional to the time that the rectal infusion was kept up. This reduction in acetonuria kept up for some time, and in addition the glycosuria was diminished. The sugar given by rectum may be better used because it goes at once into the general circulation instead of by way of the portal vein.

SURGERY

UNDER THE CHARGE OF

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Tincture of Iodine in the Treatment of Surgical Tuberculosis.—Franke (*Zentralbl. f. Chir.*, 1911, xxxviii, 953) says that this use of the tincture of iodine has not been recognized in surgery. In every operation on surgical tuberculosis in which the diseased focus is opened, there is always the danger of infecting the sound tissue with the tubercle bacillus. This applies particularly to suppurative bone and joint disease. Various efforts have been made to overcome this danger. Phelps and v. Bruns filled the wound cavity with pure carbolic acid and washed out the excess with alcohol. Burning with the Paquelin cautery or with boiled oil has been employed, and Sprengel has rubbed iodoform and calomel into the wound. Franke during the last nine or ten years has been employing tincture of iodine for disinfection of the wound after operations for bone tuberculosis, and more frequently for tuberculosis of the soft tissues. After chiselling and curetting away the tuberculous focus, or after excising a joint, he stops the hemorrhage as carefully as possible by tampon, ligation, or torsion of the vessels, and then applies over the whole wound surface strong tincture of iodine. He fills the cavity with it and then withdraws it after one or two minutes, with a syringe. In small wounds he uses merely a piece of gauze for the purpose. In some cases he drains with a rubber tube, and in others he closes the skin wound completely, trying to obtain healing by means of the blood clot. This was not always successful. He has not seen any disadvantages from the use of this method, except in one case, in which a sequestrum of bone led to the formation of a fistula of long duration. Healing by first intention is not prevented by the use of tincture of iodine in bone tuberculosis and is rather favored in soft tissue involvement, especially when the application of the iodine is long continued and the effect is intense. This is because the later hemorrhage is not so severe from the soft tissues as from bone. The hemorrhage has the virtue that it counteracts a too strong effect of the tincture of iodine, which has itself a hemostatic effect.

The New Ruggi Operation of Making a Double Opening between the Stomach and Jejunum by a Gastro-enterostomy.—Rocchi and Stoppato (*Zentralbl. f. Chir.*, 1911, xxxviii, 955) say that Ruggi teaches

and performs the operation of making a double communication between the stomach and jejunum, usually on the posterior wall of the stomach, but does not exclude the Wölfler operation of making the openings in the anterior wall. The object of the double opening is to prevent the development of a vicious circle. With this method one can make a free communication between the stomach and jejunum and can make an extensive application of the serous surface of the one to that of the other. Each opening is 3 to 5 cm. long and they are separated from each other by about 2 cm. The proximal opening may be placed in a vertical direction, as Richard-Cheuvrier, Moynihan, and Kausch recommended, and the distal opening in a transverse direction, parallel to the greater curvature of the stomach. Ruggi usually places both openings in the transverse direction.

Perforated Gastric Ulcer and its Relation to the Neutrophilic Leukocytes.—Mannheimer (*Mitt. a. d. Grenzgeb. d. med. u. Chir.*, 1911, xxiii, 553) says that the inflammatory leukocytosis in a perforating gastric ulcer case, in the beginning as well as in the further course of the disease, shows a changing picture. It is an apparently irregular, at any rate not so clear a picture as occurs in appendicitis, which is an inflammatory process from the beginning. This changing relation is explained as follows: The leukocytosis first appears with the participation of the peritoneum in the inflammation. Often, however, after a gastric perforation the inflammation is mild. The perforation may take place into the free peritoneal cavity, but the infection soon localizes itself to a portion of the cavity with the development of an encapsulated abscess. According to the varying virulence of the infection the process extends more or less widely and the stomach contents is extravasated into the abdomen. All these have a very variable influence on the blood picture, so that it assumes a special importance and may be a valuable aid in determining the character of the infection. The diagnosis of a perforating gastric ulcer is often much less dependent upon the symptoms of peritonitis than upon the other symptoms. With the establishment of the diagnosis operation is indicated. The inflammatory leukocytosis is of value for the prognosis in the beginning, but more especially in the further course of the disease. Here the leukocyte blood curve is of value. It gives information concerning the increase and decrease of the virulence of the inflammation and concerning the resistance of the body. It is also an important guide for treatment. The inflammatory leukocytosis deserves the consideration in connection with perforation of the stomach that is given to it in many other conditions.

Leverage Extension.—Deutschlander (*Zentralbl. f. Chir.*, 1911, p. 1053) says that the method of nail extension in fractures has been employed for the purpose of traction only as its name implies. There are many forms of fracture in which the strongest traction will not reduce the deformity. In these it has been necessary to use leverage, torsion, and lateral traction. Whenever the fragment offers a suitable place for the application of a combined traction, which is the rule in diaphyseal fractures, its employment offers no difficulties, and it may obviate the necessity of an open operation in some cases. By

placing a nail in both fragments, a firm hold of each is obtained and a direct correcting pull may be exerted on both. By inserting a lever between the two nails a powerful leverage effect can be obtained. After proper preparation of the fracture region, and with local or general anesthesia, a good nickel-plated steel nail can be driven into each fragment. A dressing should then be applied, the heads of the nails being permitted to protrude beyond the dressing. Longitudinal traction is applied directly to the distal fragment. A lever is inserted between the two nails. The form of lever employed by Deutschlander is illustrated. It consists of a simple rod, bent downward like a hook, where it grasps the distal nail from above, to prevent sliding, and passing backward under the proximal nail to curve upward in a half circle, where it ends. Traction by rope and pulley is made from the free upper end of the curved rod on the proximal fragment, and, as already stated, directly from the nail in the distal fragment. The effect is to turn the fragments in the desired directions, and thus to correct the deformity. If the nails are made to perforate the fragments, the same apparatus may be applied on both sides. This method was employed in the case of a fracture of the lower end of the radius, of thirteen weeks' duration. Firm union had taken place with the lower fragment completely displaced on the dorsum of the radius and turned about 90 degrees on its axis so that the wrist-joint surface looked obliquely upward. Marked ankylosis of the wrist-joint, with very little flexion and extension and no rotation, were present, and there were severe sensory disturbances from pressure of the nerves over the fragments. Under vein anesthesia the fragments were separated with a periosteal elevator, and the leverage extension was applied. After twelve days the nails were removed and the deformity had been reduced. Ordinary treatment with massage and passive movements was followed by almost complete return of motion with disappearance of the sensory disturbances.

The Ejaculatory Ducts in Hypertrophy of the Prostate and the Sexual Functions after Freyer's Prostatectomy.—Legueu and Papin (*Ann. d. mal. d. org. gén.-urin.*, 1911, ii, 1249 and 1356) present a study of this subject and report nine operations for this condition. In summarizing the results they say that in only 1 case was erection suppressed completely, and very slightly in another. Erection was normal and the sexual relations were performed in the other cases, but there was ejaculation to the exterior in only 3 cases. Suppression of the sexual appetite occurs only in the old and very feeble subjects. Erection appears to be preserved in the great majority of cases. The suppression of ejaculation is explained by the fact that in many cases the ejaculatory canals are broken. It therefore results that the orifice in the prostatic cavity is contracted, deformed, and may be obliterated, so that there may be retention of the spermatic fluid. It is probable that in many cases in which ejaculation of the fluid to the exterior does not occur, it takes place into the bladder. This ought to be especially true in those cases where there is rupture of the ejaculatory ducts, the orifices of which open into the prostatic cavity, the latter forming a portion of the bladder. External ejaculation requires the preservation of the verumontanum, which is a part of the floor of

the prostatic urethra. The organism is preserved which contributes to make us believe that ejaculation occurs internally. These facts agree perfectly with what we know of the surgical anatomy of prostatic hypertrophy. The operation is performed entirely internal to the urethra and the nerves of the genital function are not disturbed. A certain number of the patients asserted that they had somewhat recovered their youthfulness. It is very plausible that the removal of an adenoma which has been compressing the ejaculatory canals, the seminal vesicles, and prostate, may give to the sexual functions renewed vigor. There still remains enough of the accessory genital glands to produce the emulsifying fluid for the testicular secretion. What is more astonishing is, that the ejaculation may occur externally.

The Surgical Treatment of Pulsating Exophthalmos due to Arteriovenous Aneurysm between the Internal Carotid and Cavernous Sinus. A New Method.—Zeller (*Deut. Ztschr. f. Chir.*, 1911, cxi, 1) says that the common carotid on the side of the wounded internal carotid and cavernous sinus should be compressed systematically in an effort at curing the aneurysm and especially as a preliminary to ligation of the common carotid. As a result of the compression the collateral circulation will be improved, the heart will become accustomed to the greater work put upon it, and a test will have been made as to whether the patient can tolerate the shutting off of the carotid current. If brain disturbances occur after continued compression treatment, then the ligation of the common carotid is contraindicated. If success does not follow the compression treatment, the internal carotid on the side of the aneurysm should be ligated as near as possible to the base of the skull in two places and divided between. Ligation of the external carotid does not protect against recurrence, but interferes with the blood supply of the eye in case the ophthalmic artery is occluded, and therefore, should not be done. Depressing and cachectic conditions of any kind require preliminary supporting treatment, a failing heart being strengthened as much as possible. In patients of this kind, aged over forty years, ligation should be limited to the most severe cases and is only then to be permitted after systematic compression if the common carotid is found to give rise to no brain disturbances. In strong young people and in children, the ligation is to be done, as a rule, under local anesthesia. In idiopathic exophthalmos, in old people, and when arteriosclerosis is demonstrable or supposed to be present, and in traumatic exophthalmos, the systematic compression of the common carotid and careful performance of the ligation is of special importance. If, after long-continued compression of the carotid, no brain disturbances arise, careful ligation in spite of old age, is permissible. Threatening dangers after ligation are to be combatted with heart stimulation. Phlebotomy may be tried for the relief of the heart. In recurrence of the aneurysm after ligation, in mild, unilateral cases, especially when compression of the aneurysmal ophthalmic vein causes the noise to cease, excision of the same may be tried, but it is to be borne in mind that healing can occur only by the undesirable thrombosis of the cavernous sinus. In severe cases, in the bilateral variety with high grade disturbances of sight and torturing conditions, besides the ligation of the internal carotid in the neck,

intracranial ligation of the internal carotid should be done, and if possible proximal to the giving off of the ophthalmic artery. The patient should be strengthened as much as possible. Narcosis is necessary, and the operation is to be performed with as little loss of blood as possible. The operation itself is severe, but there is no danger on the side of the circulation of the brain. If the ligature can be placed only distal to the ophthalmic artery, then after the ligature is applied, the next lying portion of the ophthalmic artery should be destroyed by crushing. The ligation of the second carotid is to be strictly avoided, since experience has shown that it is especially dangerous, and upon anatomical and physiological grounds can have no healing effect.

Investigations Concerning Fat Embolism.—Groendahl (*Deut. Ztschr. f. Chir.*, 1911, cxi, 56), after a thorough study of the subject, says concerning the treatment that the prophylaxis of fat embolism from the usual bone injuries is based upon the fact that it is especially liable to occur during or after a severe transportation. The prophylaxis, therefore, should consist in the avoidance of long transportation, changing of the dressings during the first few days, and any massage. In connection with orthopedic operations the therapeutic measures are different. Here the conditions causing the fat embolism are osteoporosis and atrophy of the inactive bone. Bruising and pressing of the bones together should be avoided as much as possible. It will probably be useful to loosen up the Esmarch bandage slowly. This agrees with animal experimentation, since the animals can tolerate much more fat when it reaches the lungs slowly. A scientific therapeutic effort is that performed by Wilms in one case with success. He made a fistula in the thoracic duct upon the theory that the fat reached the lungs through the lymph paths. Later investigations by Fritz corroborated Wilm's idea. He showed in animals that through the fistula much fat escaped in large drops after bone injuries. The operation is, therefore, justified theoretically. It may be performed in cases where severe brain disturbances are present. It is known that cases with very severe brain disturbances may get well. The dangers of the operation are relatively slight, and the permanent thoracic fistula can be obliterated. Where beginning symptoms of fat embolism can be diagnosticated, the operation should be performed as quickly as possible.

Experimental Investigations Concerning Extradural Anesthesia.—Lawen and von Gaza (*Deut. Ztschr. f. Chir.*, 1911) say that the dose of novokain (0.03 gm. per animal kilogram) which by intradural injection causes the death of the animal, by extradural application causes no change in the blood pressure or only a transitory increase, never, however, a marked lowering of the blood pressure. Changes in breathing or of the corneal reflexes were not observed. The same dose of novokain (0.1 gm. per animal kilogram) which by intramuscular injection, caused no change in the blood pressure, breathing, or corneal reflexes, by extradural injection caused marked lowering of the blood pressure, cessation of the respiration and death of the animal. The toxic dose of the anesthetic by extradural injection had a considerably deeper effect than by intramuscular injection. The associated disturbances from extradural novokain injections are due to the rapid

absorption by filtration, which is aided by the increased pressure in the extradural space. The addition of adrenalin does not prevent these by-effects. They may be prevented by making the extradural injection as slowly as possible. These experimental observations agree throughout with the clinical findings. In the Leipzig clinic the extradural anesthesia is now obtained by injecting the necessary amount of novokain bicarbonate very slowly, taking from one to two minutes to complete it.

Surgical Treatment of Fistula in Ano without Mutilation of the Sphincter.—MacKenzie (*Annals of Surgery*, 1911, liv, 360) treated by the following operation two old cases of fistula in ano, one of forty-six and the other of four years' duration, with success. In the former case, many operations and in the latter, two or three, had been previously done without success. The patient is prepared in the most careful way as for any major operation on these parts. The sphincter is completely dilated. The internal orifice of the fistula is minutely examined and with a proper instrument is cautiously dilated. After dilatation, the mucosa is uplifted and pared with a curved scissors in the direction of the long axis of the bowel, and with a small knife or fine scissors the circumference of the muscular layer is then trimmed and vivified. If need be, the opening may be incised or split in the direction of the circumference of the sphincter. After this has been done a few interrupted sutures of iodized catgut are introduced in the muscular layer at right angles with the sphincter, tied, and divided. The mucous membrane is then sutured with interrupted chromic catgut or silk sutures, properly spaced. If more than one orifice exists, of course, the same procedure is followed. A flap is made on the side involved, beginning by making a small semilunar incision just beyond the border of the external sphincter, dividing the parts down to the fistulous tract, the latter being divided flush at its point of emergence from the bowel. The incision is extended from both ends of the first incision outward and made large and deep enough to include, if possible under the eye, all visible and accessible branching tracts. The exigencies of the case may require sometimes the lifting of one or the other of the buttocks in its entirety. In one case it was necessary to make a complete and partial resection of both buttocks in order to reach the deepest and most distant branching tracts. The opposite side of the rectal opening is now attacked, and after all doubtful tissues have been removed the rectal wall is infolded once or twice over the line of sutures within. The greatest care must be exercised in removing all doubtful tissues. If need be, the cautery could be used for their complete destruction, or substituted entirely for the suture of these parts. The exposed flap is next attacked with knife or large pointed scissors curved on the flat, and the original tract, its branches, and the entire fistulous zone including every branching tract resected. Careful search will be made in the ischiorectal fossa and perirectal spaces for any concealed tracts. The whole field is then carefully flushed with normal salt solution, and if need be, antiseptized and the fat layers sutured with buried catgut so as to close all dead spaces. In many cases the entire wound may be closed as in the case of breast amputations, or a small drain may be left for twenty-four or forty-eight hours.

THERAPEUTICS

UNDER THE CHARGE OF

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Aspirin as a Remedy for Cough.—Ebstein (*Deutsch. med. Woch.*, 1911, xxxvii, 1476) has had good effects in the treatment of cough with aspirin. He has seen it give relief when codeine had failed. He believes that it does more than give relief, that it tends to cure and materially shorten the duration of the cough.

The Action of Vasotonin.—Schaltenstein (*Deutsch. med. Woch.*, 1911, xxxvii, 695) has used vasotonin in increased blood pressure due to aortic insufficiency, arteriosclerosis, and aneurysm. About fifteen injections were given as an average treatment, usually every day or every other day. The lowering of the blood pressure was not very noticeable, and the effects were not permanent. However, in a number of patients cardiac attacks were much diminished and in some this result occurred after other remedies had failed. The remedy had no effect at all upon high blood pressure due to a chronic nephritis. No untoward effects were noted from its use.

Iodival.—Bayer (*Therapie d. Gegenwart*, 1911, lii, 335) says that in his experience iodival, in spite of its high iodine content, has not given rise to symptoms of iodisin after the continued use of it in doses of 0.3 gram three times a day. It seems to have a special affinity for nerve tissue, and animal experiments have shown that both fat and nerve tissue are rich in iodine after the administration of iodival. Bayer has noticed clinically very good results in brain affections treated with iodival, and he believes that they may be explained by a selective action of iodival upon nerve tissue. Iodival has no unpleasant taste and does not give rise to gastro-intestinal irritation.

The Use of Foods Rich in Inulin in Diabetes.—Strauss (*Therap. d. Gegenwart*, 1911, lii, 347) advocates various vegetables rich in inulin for the dietary of diabetes. He believes that they are especially valuable for the treatment of severe cases with acidosis. Besides their content of carbohydrate, that seems to be better tolerated than ordinary carbohydrates, they offer a source of vegetable proteid. Among these he mentions artichokes, Jerusalem artichokes, dandelion roots, dahlia tubers, and various members of the Lelianthus family. These may be given as vegetables, or in soups, and he suggests various methods of preparation to render them palatable. Inulin has also been given in pure form, but it is too expensive for ordinary use. From some of these vegetables a flour has been prepared, as in the case of that derived from Jerusalem artichokes.

The Use of Salicylates in Rheumatism.—Alex. Lambert (*Jour. Amer. Med. Asso.*, 1911, lvii, 898) says that, in using salicylates in rheumatism, if within forty-eight hours a distinctly beneficial action is not obtained with the form of salicylate that is being used for that patient, some other form of salicylate should be employed. Most patients are easily irritated by salicylic acid and their stomachs soon reject it, yet these same patients will readily take sodium salicylate with no disturbance. Sodium salicylate, if given in solution with an excess of alkali, is infinitely less irritant to the gastric membrane than when given in powder form. Some patients cannot take sodium salicylate, and yet they tolerate oil of wintergreen in large doses and rapidly respond to it. This natural oil of gaultheria is no longer on the market, but the oleum betulæ, or oil of sweet birch, contains the same natural methyl salicylate. The natural salicylates seem to be less irritant and are more active than the synthetic salicylates. Synthetic methyl salicylate is not suitable for internal use, and should only be used externally. Lambert mentions salol, salicin, and salophen as forms of salicylates that may benefit when the more usual remedies fail. He particularly recommends salicin for rheumatic affections in children and in the aged as the form which is the least depressing and from which the most benefit seems to be obtained. Results from the use of aspirin in rheumatism have been disappointing to Lambert personally, although it is highly recommended by some. He mentions the hypodermic method of giving salicylates as recommended by Siebert. The results of treatment by this method are excellent, and this method may prove of advantage in those patients who cannot take salicylate by mouth. Lambert recommends highly a form of salicylate the use of which seems to reduce to a minimum the irritating and toxic symptoms. This salicylate is prepared as follows: Oleum betulæ is saponified either by superheated steam or caustic alkali; the resulting methyl alcohol is driven off by heat and the resulting salicylate is decomposed by sulphuric acid and washed until free from sulphates. After the salicylic acid is purified by recrystallization it is mixed with an excess of sodium bicarbonate and made into tablets with a sugar binder. These tablets are freely soluble in water with a pleasant acid taste and with a free elimination of carbon dioxide. Lambert says that this form of salicylate enables one to get a large amount of active salicylate into the circulation at once in the least toxic and most effective form of the natural salicylate. It is unforunately doubtful whether they will be in general use because of their expense. It is an exceedingly active and useful form of salicylate, however, with a maximum of rapidity of absorption, effectiveness after absorption, and a minimum of toxic action.

The Use of Arsenic in the Treatment of Chlorosis.—Seiler (*Deut. med. Woch.*, 1911, xxxvii, 1340) relates the results obtained by him in the treatment of 33 patients suffering from chlorosis. Thirteen of these patients were treated with arsenic alone, 12 received iron only, and the remaining 8 were given a combined treatment with both iron and arsenic. Seiler gave the arsenic in the form of arsenous acid in doses of from 0.005 gram to 0.01 gram a day either in pill form or by subcutaneous injection. The patients treated with arsenic alone derived

little or no benefit. The hemoglobin percentage after two or three weeks of this treatment increased slightly, but there was an actual fall in the number of red blood cells. In addition to this lack of improvement, untoward symptoms frequently occurred from the use of the arsenic. Consequently, Seiler believes that arsenic alone has no therapeutic effect upon chlorosis. Iron alone was given in the form of a modified Blaud's pill for four weeks. The hemoglobin percentage increased markedly and the number of red blood cells rose to nearly normal. The average of 49 per cent. hemoglobin rose to 87 per cent. and the number of red blood cells increased from 4,000,000 to 5,000,000. The patients treated with iron and arsenic in combination received in addition to the Blaud's pill an average dose of 0.006 gram of arsenous acid a day. After four weeks of this combined treatment the average hemoglobin percentage rose from 37 to 96 per cent., and the red blood cells increased from 3,000,000 to 5,100,000. Seiler believes that this combination of iron and arsenic has a more rapid and more complete curative action than iron alone.

The Practical Significance of the Wassermann Reaction in the Treatment of Syphilis.—Plehn (*Berlin. klin. Woch.*, 1911, xlviii, 1544) believes that the Wassermann reaction is by no means a reliable guide for the treatment of syphilis, especially in its late manifestations. He had the serum of 200 patients tested for the Wassermann reaction with the examiner ignorant of the clinical history of the patient. The results were not in accordance with the clinical history in many instances. Nine patients who gave a positive Wassermann reaction repeatedly had reached an advanced age without ever having had any manifestations of their syphilis after the first infection. He also says that the Wassermann reaction may become negative even when marked manifestations are persistent or syphilitic symptoms may develop a considerable time after a negative complement deviation test. A negative reaction, therefore, does not always indicate a cure, and Plehn believes that parasyphilitic symptoms especially may develop a long time after a negative reaction. The reaction may be positive for years while the patient is entirely free from clinical symptoms, and, according to Plehn, this positive reaction cannot be considered as proof of the syphilitic nature of clinical symptoms developing during this time. The symptoms may or may not be due to the syphilitic virus. The author says that the Wassermann reaction is only one symptom of syphilis and that the diagnosis of active syphilis must not rest upon that alone, although he believes that it often helps in doubtful cases. He cites the case of a young man who, because of the knowledge of a positive Wassermann reaction, although he had no clinical symptoms of syphilis, was so much depressed that he committed suicide. At the autopsy not the slightest evidence of syphilis was found. Plehn summarizes his views by the statement that complement fixation should be used with great care in diagnosticating symptoms occurring during late periods of syphilis because it often proves to be an erroneous guide. This fact is especially true in the differential diagnosis in diseases of the central nervous system. He also believes that complement fixation alone can never be an indication for or against specific treatment except when it determines the diagnosis of syphilis in the early stage.

The Crotalin Treatment of Epilepsy.—Spangler (*New York Med. Jour.*, 1911, xciv, 517) gives a tabulated report of 36 cases of epilepsy treated with hypodermic injections of rattlesnake venom. The present article confirms the results as related in a preliminary report on the same subject. Spangler says that the venom treatment is indicated in the so-called idiopathic form of epilepsy. Under the crotalin treatment the character of the convulsions is modified, the interval between the attacks lengthened, and the mental and physical condition of the patient is improved. It is important to use a solution of the venom of definite and uniform strength. It is most essential to determine the strength of dose necessary to cause a satisfactory local reaction, that will produce a systemic effect sufficient to control the convulsions. Experience and observations as to the character of the local reaction are of great value in determining the proper dose for each individual case. Spangler gives the details of the technique for the injection and indicates his method of ascertaining the proper dose for the individual case. He says that organic epilepsies, including those forms arising from traumatic lesions of the skull or brain, such as tumors, cannot be expected to yield to the venom treatment. Likewise, no influence on alcoholic epilepsy or convulsions arising from uremic or eclamptic conditions can be looked for. Although only three of the cases reported resulted in cures, yet the general improvement in the patients' mental and physical condition was so marked that Spangler warmly advocates this method of treatment in all cases of idiopathic epilepsy.

Experiments on the Relation of the Thyroid to Diet.—Hunt (*Jour. Amer. Med. Assoc.*, 1911, lvii, 1032), acting upon the hypothesis that certain diets have specific effects on the activity of the thyroid gland, has endeavored to support this by animal experiments. The method employed is based on the increased resistance which mice show to acetonitril after the feeding of thyroid. Earlier experiments had shown that the resistance to this poison was much greater in the case of mice that had a diet of oatmeal, or of oatmeal and liver, than in the case of those that had a diet of eggs, crackers, and milk. The results were in entire harmony with the above hypothesis, although Hunt does not consider the experiments sufficiently numerous or varied to be entirely conclusive. In his summary he says that these experiments afford additional experimental support for the view that certain diets have specific effects on the thyroid glands of some of the lower animals. It is probable that analogous relations hold for human beings. Although it is possible that the effects differ in different classes of animals, it would be interesting to determine if, in cases of hypothyroidism, the administration of oatmeal and liver, for example, would have a favorable influence, and if the withholding of them from patients with hyperthyroidism would be found advantageous. The most promising class of cases for such observations would be the mild degrees of thyroid derangement, such as those recently described by Kocher in his Nobel lecture.

PEDIATRICS

UNDER THE CHARGE OF

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Epidemic Summer Diarrhea and Vomiting.—HAROLD WALLER and GERALD WALKER (*Brit. Med. Jour.*, 1911, No. 2646, p. 594) report an epidemic of summer diarrhea as seen in the East London Hospital for Children. About one-third of the children seen in the out-patient department suffered from this condition. From July 1 to August 18 there were 125 admissions for this condition. Of these, 50 died and 75 were discharged cured. The large proportion of cases were bottle-fed and marasmic. Severe attacks in breast-fed babies were wholly exceptional. Condensed milk seems to have been the staple article of diet among these children, although the barley water so often an ingredient is believed to be sufficiently dangerous in itself to be responsible for a great deal of the trouble. This is due to the strange recipes for making the barley water, and to its being allowed to stand on a hot day in dirty jugs. The majority of cases occurred in infants from four to twelve months old and considerably under the normal weight. Rickets were common in the older children. In nearly all the cases there was pyrexia. The general condition exhibited sunken eyes, depressed fontanelles, skin dry and wrinkled, great loss of subcutaneous fat, and sunken abdomen. Abdominal distention was uncommon. The tongue and palate were very dry and often covered by thrush. While the high mortality suggests poor treatment before admission, the attack in many cases followed gross misfeeding. The general treatment is as follows: On admission the stomach is washed with a 0.9 per cent. saline solution, after which the vomiting usually ceases absolutely. The bowel is irrigated with the same solution until clear. If collapse or shock is present, a mustard bath or mustard pack is given. A subcutaneous infusion of normal saline or a 5 per cent. solution of glucose in normal saline is then given for several hours. This last treatment is of the greatest importance, but must be given at about 105° F. to be readily absorbed. An inverted vacuum flask is fitted with a rubber stopper containing two holes, one for a glass tube admitting air, the other tube, of the "two-way" kind, carries the fluid through two pieces of rubber tubing 8 inches long, to which are attached small silver infusion needles. The child is placed on its back and the limbs secured with bandages to the side of the cot. The abdomen and thighs are prepared for surgical procedure. A board with a hole in the centre supporting the inverted flask is laid across the side of the cot. The apparatus is sterilized and the flask filled with the requisite amount of saline at 120° F. The needles after insertion are covered with sterile gauze. About 7 to 10 ounces of saline are employed and will take two hours to run in, an occasional inspection of the apparatus being sufficient. Frequent repetition of the subcutaneous infusion is necessary

to replace the loss of fluid in the tissues. Water, preferably hot, is all that is given for twenty-four hours. Whey has been extensively tried as the first food and answers well, but tends to cause a dirty condition of the mouth. A 5 per cent. solution of glucose, to which albulactive may be added, is useful. Milk, freely diluted with water, and with only the addition of sodium citrate, is tried only when the diarrhea subsides. Open air treatment during convalescence is invaluable. Of drugs, calomel in repeated small doses, castor oil, ℥ij to ℥v, and opium are the most valuable. Bismuth is most deadly in anything but quite the last stages. In no instance has the complaint been contracted by children suffering from other conditions, although in the same ward. Bronchopneumonia was the cause of death in 8 cases. Excellent nursing is absolutely essential for good results.

Typhoid Fever in Childhood: An Analysis of One Hundred Consecutive Cases.—Eric Bellingham Smith (*Brit. Jour. Child. Dis.*, 1911, viii, 390) reviews 100 consecutive cases of typhoid fever in children, aged from one to twelve years. The main features of the disease at this age are especially discussed. In the great majority the attack was an isolated one in the family, and its origin was untraceable. Sex apparently has no influence, as 51 of the cases were girls and 49 were boys. Age, however, is an important factor. No case in this series was under one year, but from this period to twelve years there was a steady increase in the number of children infected. The duration of the disease was variable. In 88 cases the time of onset was fairly well established. Of these 88 cases, 6 lasted only eight to twelve days, 43 from fifteen to twenty-one days, and 39 for twenty-one days and over. The shortest illness was eight days, and the longest fifty days. The disease is less serious in children than in adults. Vomiting at the onset is fairly common, and occurred in 27 per cent. of the cases. More often this onset is gradual and the symptoms differ little from the adult type. Severe onsets at times simulate meningitis. Of the 100 cases, 8 per cent. exhibited this meningitic type and 16 per cent. showed marked mental irritability. Diarrhea frequently ushers in the disease, but rarely continues severe. A fourth type exhibits prominent pulmonary signs, as diffuse bronchitis, with poorly marked physical signs, but a high pyrexia. Headache, bronchitis, and slight diarrhea, with gradual emaciation, occasionally form the only symptoms. Occasionally the disease exhibits itself under the guise of other ailments. In 2 cases a marked tonsillitis was the most prominent symptom. In 2 others marked emaciation was the only feature. Again, cases occur with scarcely any evidence of ill health. The symptoms during the course of the disease presented very little difference from those in adults. In this series the rose spots were present in 64 per cent. of the cases and splenic enlargement in 51 per cent. The stupor and coma of adults rarely occurs in children. Delirium, usually nocturnal, is present. Subsultus is uncommon. Pulmonary symptoms are often absent. Emaciation is a constant feature. In this series 17 per cent. showed myocardial trouble during the third week, and a slight affection of this nature is probably the most common complication of typhoid fever in children. Nephritis is rare, while otorrhea and deafness are not uncommon toward the end of the illness. Abscesses and

boils are not uncommon at the end of the illness. Hemorrhage and perforation are infrequent. In this series 50 per cent. recovered at the end of the second or the beginning of the third week, showing that slight swelling or superficial ulceration of Peyer's patches is probably all that occurs in these cases. In the two fatal cases of perforation the children were aged eleven and twelve years respectively. Hemorrhage from the bowel occurred in 7 cases, in 4 of which it was slight; in 3 it was severe, but not fatal, and showed the usual collapse symptoms. In these 3 cases the hemorrhage occurred during the fourth week. The stools in 22 per cent. of the cases were typical, in 18 per cent. constipated, in 17 per cent. green and offensive, and in 34 per cent. there was some degree of diarrhea. Convalescence is rapid, constipation being usually the only difficulty; 11 per cent. of cases had a typical relapse. The pyrexia of typhoid in children is as atypical as the stools, and may be continuous, intermittent, and irregular, or remittent. The prognosis is good. In this series there were 7 deaths from the following causes: Perforation, 2; toxemia, heart failure, 2; pneumonia, 1; suppurative parotitis, 1; pneumonia, empyema, cancrum oris, 1. In 76 cases of this series, 58 gave a positive Widal reaction. Drugs have no influence on the course of the disease. The diet should be milk, plain, citrated, or peptonized. Constipation is relieved by beef tea and chicken broth in the dietary and enemata. Strychnine and brandy control myocarditis. The toilet of the mouth is most important, and antiseptic remedies should be constantly applied. High temperature and delirium are treated by sponging with tepid or cold water. Cold baths and ice are not recommended.

Deafness from Mumps.—Oscar Mauthner (*Wien. med. Woch.*, 1911, lxi, 2090) calls attention to the severity of deafness occurring as a complication in mumps. In 1898 Gallavardin collected over 51 cases of complete, permanent deafness occurring in acute epidemic parotitis. In the majority of cases this condition arises suddenly during the course of the disease, and is ushered in by a roaring or rushing sound in the affected ear, developing rapidly into complete and permanent deafness. There is rarely local pain and almost never an affection of the middle ear. The onset is further characterized by severe dizziness, loss of equilibrium, nausea, vomiting, and headache. These symptoms, denoting involvement of the vestibular apparatus, usually accompany the deafness or occur several days later, but in some cases they appear even before the swelling of the parotid gland. Mauthner reports the case of a woman with bilateral epidemic parotitis. On the first day there was a ringing in the left ear, which increased to a roaring noise, and forty-eight hours later there was absolute deafness in the affected ear. Dizziness and nausea appeared forty-eight hours later. The dizziness and unsteady gait persisted for six weeks. The roaring noise and deafness have continued for eight months. A treatment of pilocarpine internally and the faradic current locally had no effect on the condition. After a lengthy discussion of the various factors and clinical manifestations of the reported cases, Mauthner concludes that the process in this type of deafness is similar to that of an acute infectious neuritis—a neuritis of the auditory nerve.

OBSTETRICS

UNDER THE CHARGE OF

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The Treatment of Excessive Vomiting of Pregnancy.—Martin (*British Medical Journal*, July 8, 1911) describes the method of treatment employed at the Glasgow Maternity in cases of excessive vomiting of pregnancy. On admission a thorough examination was made, and in most cases some cause was found which affected the patient's general health; bad teeth and chronic constipation were associated in every case. The patient was strictly confined to her bed, was encouraged, and told that she would recover; the stomach was thoroughly irrigated with the tube and warm water at 100° F. Large quantities of mucus were obtained. Sips of water were allowed that night and an enema of soap and water given in the morning. A test meal was given next morning and withdrawn one hour after by the stomach tube. In no case was the test meal returned, and in one patient no vestige of the test meal was obtained by again irrigating the stomach. In all but three cases the free hydrochloric acid and total acidity were normal. In three the quantity was slightly diminished. The motor activity of the stomach was tested and found normal and microscopic examinations of the stomach washings were negative. Patients were fed on peptonized milk and milk and soda water and as soon as possible a light diet. A powder containing 1 grain of mercury with chalk and 3 grains of sodium bicarbonate was given three times daily. Magaesium sulphate in hot water was given every second morning if needed. Enemata were used as necessary. The septic condition of the mouth was treated by carbolic acid solution, 1 to 80. The patients were urged to drink large quantities of milk and soda, weak tea, or other alkaline drinks. In 16 cases the method was successful, the average stay in the hospital being seventeen days. In one case there was retroversion of the uterus, but this was not interfered with, and the patient made a good recovery. In 5 cases there was a well-marked acetone odor. Fifteen of the patients were admitted during the winter months when the climate was cold and damp.

Tincture of Iodine as a Disinfectant in Obsteric Practice.—Schmidt (*Zentralbl. f. Gyn.*, 1911, No. 25) in 52 cases employed tincture of iodine as an antiseptic. These cases included artificial dilatation of the cervix by various methods, breech extraction, version and extraction, including twin pregnancy and placenta prævia, the application of forceps, embryotomy of various sorts, and manual removal of the placenta and fetal appendages. The ages of the patients varied from eighteen to forty-three years. In 15 the puerperal period was without the slightest elevation of temperature; in 16 the temperature was abnormally low; in 3 it reached 99.5° F.; in one, after artificial removal of the placenta, when the patient had been examined by a midwife outside, the temperature reached 101° F., and in one case dying of eclampsia and ane-

mia, the patient's temperature reached 102° F. In 15 cases stitches were taken in a torn perineum and in episiotomy wounds. These cases also healed by first intention and remained without fever. No eczema or other irritation of the skin was observed.

Intra-uterine Cry.—Konopha (*Zentralbl. f. Gyn.*, 1911, No. 25) describes the case of a multipara four weeks before her actual time of confinement, who suffered from edema in the lower extremities, albuminuria, and scanty secretion of urine. The pregnancy was interrupted because of the abdominal distention, the patient suffering with albuminuria. When the membranes ruptured considerable amniotic liquid escaped; the case was found to be twins, the first child presenting by the breech. To hasten delivery, the physician drew down upon one leg of the child, when it was heard distinctly to cry in the uterus. The child was immediately extracted and the umbilical cord found coiled three times about the neck, and readily loosened. The child was asphyxiated, but very soon revived. On introducing the hand into the uterus to extract the second child, air escaped. The mother and children made a good recovery without complications.

Forty Cases of Placenta Prævia.—Edgar (*Amer. Jour. of Obstet.*, July, 1911) gives his results in the treatment of 40 cases of placenta prævia—10 central, 9 partial, 21 marginal. Seventeen of these were ambulance or emergency cases, first seen at the beginning of bleeding. In 23 bleeding had lasted from a few hours to several days. Seventeen of these patients had received various treatments before entering the hospital, and 23 were treated exclusively by the hospital. In 29 cases the cervical dilatation was two fingers or less when the patient was first seen. The treatment employed was cervical and vaginal gauze packing in 32 cases; De Ribe's bag in 3 cases; Pomeroy's bag in 7; bimanual dilatation as a preliminary measure in 2, gauze packing in 10. Labor was induced in 9 cases. The methods of delivery were version and breech extraction in 20 cases, the use of forceps in 6, breech extraction without version in 5, spontaneous delivery in 8, making, with the one case not delivered, 40. The uterus was tamponed after delivery in all cases. The maternal mortality was 7.5 per cent., the fetal mortality 32.25 per cent. The conclusion was reached that cervical and vaginal packing with gauze is efficient in controlling hemorrhage, in securing dilatation. These mortality rates are thought satisfactory in cases one-half of which were ambulance or emergency cases. Version and breech extraction cause a higher infant mortality than delivery by forceps, simple breech extraction, and spontaneous expulsion.

Inflammatory Disease of the Adnexa and Pelvic Tissues in Parturient Patients and its Treatment.—Thaler, from Schauta's Clinic (*Archiv f. Gyn.*, 1911, Band xciii, Heft 3), gives the results obtained from 6000 cases of inflammatory disease of the adnexa treated by operative means. He found in the majority of cases some efforts at spontaneous cure had been made, and that often the secretion of large quantities of pus was not necessarily fatal. Although conservative measures should be used in all cases, it was found that in at least 10 per cent. these measures failed and operation only was indicated. He inclines strongly to the belief that extirpation of diseased organs is, in the long run, the only

reliable treatment. He does not believe that incision is followed by permanent improvement. He prefers to operate by the vaginal method wherever it is possible. Where, however, there are many and firm adhesions, and there is reason to believe that the appendix is involved, he would select the abdominal route, employing drainage through the vagina, in complicated cases. The abdominal method is also preferable where the position of the uterus has been greatly altered and it is desired to correct it. Transverse incision is preferable in severe cases where the operator fears infection from the rupture of a pus sac or injury to the intestine, although due allowance must be made for the prolonged healing and the risk of suppuration in the transverse wound. The appendix should at least be inspected in all cases, and if adherent or altered, should be removed. The total extirpation of the uterus followed by drainage through the vagina will give the best result in septic cases, even accompanied by injury to the bowel. His observation shows that in the majority of cases radical operation is safer, and followed by better and more permanent improvement, than if the conservative method has been followed. This remains true in many cases where it would seem reasonable to expect that conservatism in operating would give excellent results. Where conservatism is to be employed, salpingectomy, bilateral, with the leaving of one or both ovaries, ventrofixation of the uterus, and excision of the insertion of the tubes into the uterus, gives good results. When, however, the indications for drainage are clear and definite, conservative treatment should not be employed. The same decision is made in cases where the patient suffers from severe and practically uncontrollable hemorrhage. The mortality of cases treated by vaginal extirpation where suppuration was absent was 1.8 per cent., and where suppuration was present, 2.8 per cent. The general mortality of abdominal operations on the adnexa was 5.3 per cent. without suppuration, and 8.6 per cent. with suppuration. During the last three years 50 cases of tubal suppuration had been treated by the abdominal method, with a mortality of 6 per cent. A permanent result with good union followed radical operation in 93.5 per cent., while under favorable circumstances only, abdominal conservative operations were followed by permanent recovery in 72.2 per cent. When the very practical question is raised as to what treatment gives the patient the best permanent result, with ability to work and to support herself and with freedom from pain, it is found that radical operation is more successful than efforts at conservatism. When inflammation of the adnexa is complicated by pregnancy, intra-uterine or extra-uterine, or by appendicitis, or the process present is found to be tuberculous infection, the best results followed conservative treatment. It is also interesting to note that permanent infection of the adnexa rarely follows puerperal infection, and that these cases tend to spontaneous recovery.

The Best and Worst Methods of Treating Placenta Prævia.—Fry (*Amer. Jour. of Obs.*, July, 1911) considers version without extraction the best method of treating placenta prævia, and those methods which result in rapid extraction the worst and most dangerous. He lays stress upon the careful and efficient packing of the uterus with gauze, after the removal of the child, as a most valuable method of preventing postpartum hemorrhage.

GYNECOLOGY

UNDER THE CHARGE OF

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Relation of the Sigmoid to Pelvic Disease.—Barrett (*Surg. Gyn. and Obst.*, 1911, xiii, 320) calls attention to the fact that gynecological surgery had been under development for many years before the close and important anatomical and pathological relationship which exists between the pelvic organs and the appendix came to be realized, and says that while this is at present well recognized, the even more intimately related pathology of the sigmoid is only just beginning to be appreciated by gynecologists. The position of the sigmoid may vary greatly according to whether it has a short or long mesosigmoid; in the latter case it may prolapse into the pelvis, and has been found adherent to practically every known pelvic and abdominal structure. It becomes, therefore, a looped, kinked, or sacculated structure, with congenital or acquired diverticula, loaded with irritating excreta, swarming with bacteria within, and subject to bacterial invasion from without. The author considers that while the sigmoid is certainly prolific in producing pelvic disease, it is even more often involved secondarily to genital trouble. When involved in a pelvic abscess by forming part of its wall the inflammation may extend throughout the coats of the sigmoid, causing thickening and perforation, followed by a secondary infection of the abscess with colon bacilli. Much left-sided pelvic pain is undoubtedly due to adhesions, kinking, constrictions, etc., of the sigmoid, and many of these patients will be found on careful questioning to have had attacks of alternating constipation and diarrhea, or to have passed mucus or blood. In doing any intra-abdominal operation on the round ligaments it is especially important to free these organs from all adhesions, so as to prevent any traction or knuckling of the bowel. In removing thickened appendices epiploicæ it should be remembered that they may contain a lumen communicating with that of the gut, so that in removing them we may be opening the bowel, and should treat the stump accordingly. In conclusion, the author emphasizes the fact that in the performance of any laparotomy for pelvic disease conditions of the bowel ranging from adhesions to malignant newgrowths, may be met with, and that every pelvic operator should, therefore, be thoroughly equipped to do intestinal surgery.

Carcinoma of the Uterine Body.—In an article of some ninety pages in length, Heurlin (*Arch. f. Gyn.*, 1911, xciv, 402) discusses the anatomical characteristics and method of growth of corpus carcinoma, his conclusions being based on the exhaustive investigation of some 50 cases of that and allied conditions, together with a most extensive

review of the literature. He believes that this form of carcinoma always originates in one circumscribed location in the mucous membrane, and is, therefore, strictly unicentric in origin; where several distinct foci are found, even though they be of approximately equal size, he considers the condition due to lymphatic metastases rather than to a multicentric origin of the growth. The intact mucous membrane of the corpus can always be seen, at least microscopically, to have a definite limitation against the carcinoma; the former is invaded and displaced by the latter. While most cancers of the corpus are adenocarcinomata, Heurlin thinks the term "malignant adenoma" should be retained for that form in which the glandular epithelium retains its single-layered character, although this type of tumor may be as malignant as any other. The old theory that an adenocarcinoma arises from an "endometritis glandularis" must be given up, as the author found the mucosa atrophic in all his cases, with intact, normal, or cystic glands. He does not believe that primary epithelial changes exist from which a very early diagnosis of beginning carcinoma can be made, as neither morphological changes in the cells, atypical mitoses, nor atypical proliferation are of value in this respect, nor is the presence or absence of a demonstrable breaking through of the membrana propria of the glands on the part of the epithelium an available criterion. He has never found carcinoma of the corpus to extend along the mucosa into the cervix; it always stops where the character of the surface epithelium changes, at the internal os, but it may extend into the cervix deep in the muscular wall, and then reappear on the surface.

Topography of the Ureter.—In order to determine the normal course of the ureter during life, Schmidt and Kretschner (*Surg. Gyn. and Obst.*, 1911, xiii, 287) carried out a series of investigations on perfectly normal individuals, using for this purpose ordinary ureteral catheters armed with fuse wire, which because of its great pliability gives rise to less irregularities or distortions than any other substance, *x*-ray pictures being taken with the patient always in the prone position. It was found that the ureters had a very varied course in these supposedly normal subjects, some being almost straight, others S-shaped, others markedly serpentine and irregular. In some cases the two ureters ran almost parallel throughout their whole course, in others they drew quite close together in the lower portion, spreading farther apart above, etc. The authors believe as a result of these investigations that it is impossible to say whether a given shadow on an *x*-ray plate is in the course of a ureter or not unless the picture is taken with a shadowgraph catheter in place, and that the frequent atypical course of the ureter explains the ease with which this organ is injured during operations on neighboring structures.

Origin of Hydatid Mole.—Falgowski (*Monatsschr. f. Geb. u. Gyn.*, 1911, xxxiv, 290) reports a most interesting case of twin pregnancy (2 ova), in which a normal child and placenta, and an hydatid mole were delivered at term, evidently one ovum having developed normally, while the other had undergone hydatid change. There was no trace of an embryo in the latter. The author considers that this case furnishes strong evidence in favor of the view that the development of an

hydatid mole is due to some primary disease of the ovum, it not being conceivable that endometritis or any other uterine condition was the cause here, since only one ovum was affected. Moreover, the only way to explain it by a multicystic degeneration of one ovary (Marchand's theory) would be to assume a superfetation of two ova, one from each ovary, at different times, a most improbable occurrence. Neither can the development of an hydatid mole be considered due to the death of the embryo, as in the large majority of cases where, from some cause or other, death of the embryo occurs this is not followed by the formation of an hydatid mole; on the other hand, cases are known where only a small portion of the chorion has undergone this change, the remainder being normal, in which death of the fetus did not take place.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES

UNDER THE CHARGE OF

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Paresthesia of the Pharynx an Advance Symptom of Tumors of the Digestive Tract.—Pugnat (*Revue Hebd. de Lar., d'Otol. et de Rhinologie*, January 7, 1911) reports and comments upon three elderly patients who consulted him for uncomfortable sensations in the pharynx which could not be relieved by treatment. The first case was followed in six months by an inoperable cancer of the intestine; the second was followed in six or seven months by fatal cancer of the stomach, and the third, was followed in four months by a cancer of the rectum, which was removed. He therefore suggests that in all cases of paresthesia of the pharynx, which cannot be otherwise accounted for, careful exploration should be made of the gastro-intestinal tract.

Sarcoma of the Tonsil in an Infant.—Cline (*The Laryngoscope*, March, 1911) reports a case of sarcoma of the tonsil in a male child, aged twenty-two months. Two months prior to the visit it had had what was thought to be tonsillitis, which developed two weeks later into a tonsillar abscess. The abscess had ruptured and a considerable amount of purulent fluid discharged. On examination, a nodular growth was found involving the left tonsil, almost filling the pharynx. It was rather soft to the touch and bled profusely upon pressure. Microscopic inspection of a section removed revealed it to be a sarcoma. Urgent dyspnea was relieved by removing as much as possible of the growth with the cold snare and the tonsil punch, which was done without much hemorrhage. Radical operation was out of the question. The child grew rapidly worse and died in two weeks.

Sporotrichosis of the Tongue and Pharynx.—Duverger and Bain (*Revue Hebd. de Lar., d'Otol. et de Rhinologie,* April 15, 1911) report a rare case of lingual and pharyngeal sporotrichosis with menacing asphyxia from which cultures were made of the sporothrix Beurmanni. The patient was a Syrian lad some fifteen years of age, sent with a diagnosis of double periamygdalien phlegmonitis. The tongue was very much swollen and projected beyond the teeth, and was covered with a thick papiermache-like deposit more than $\frac{1}{2}$ cm. in depth. It had great physical resemblance to that of burns of the tongue from acid, especially of phenic acid. There was edematous enlargement of the buccal floor and the sublingual glands. The mucous membrane of the palate was infiltrated, somewhat pale, milky in spots, and covered with small stellate whitish patches, particularly numerous on the soft palate, the arches, the hard palate, and the pharynx. The tonsils, on the contrary, were but slightly voluminous and presented a very discrete yellowish-white deposit, as also did the internal face of the cheeks. The examination of the larynx was not practicable. There was great difficulty in respiration, in mastication, and in deglutition. As to treatment, the tongue was curetted of a mass of pale yellowish papiermache-like material of a very repulsive and putrid odor. The ulcerated surfaces were touched with strong iodo-iodurated solution, and boroöxygenated mouth washes were prescribed, and four grams of iodide of potassium administered daily, under which the patient made a rapid recovery. The sporothrix of Beurmann was recognized under the microscope and cultures made, the results of which are described and depicted in the article which, in addition, gives a summary of what is known of this rare malady.

Menthol in the Nasal Passages Dangerous to Infants.—Mayet (*Revue Hebd. de Lar., d'Otol. et de Rhinol.,* April 22, 1911) has observed two cases of asphyxia from the introduction of mentholated preparations into the nasal passages of infants, and he refers to several similar accidents reported by other writers. He concludes that menthol should be proscribed from infantile therapeutics.

Nasal Neuralgia.—Broeckaert (*Annales des Mal. de l'Oreille, du Lar., du Nez et du Pharynx,* Livraison 1, 1911) describes and depicts his method of exposing the branches of the nasal nerves and tearing them from their beds in the successful treatment of this painful affection.

Nasal Diseases following Injuries of the Head.—Ziem (*Jour. of Lar., Rhinol., and Otology,* March, 1911) expresses his astonishment that so little stress is laid upon the state of the nose and sinuses after injuries to the head. He reports in detail 3 cases in point and refers to several others. In all 3 cases there was a lesion of the right side, but in 1 only was the speech affected, although the patient was right handed. Involvement of the middle ear was present but in 1 case. Injuries to vision occurred in all of them, and various other nervous manifestations, bad dreams among them. Hemorrhage from the mouth and nose and hemilateral anosmia existing in all 3 cases was referred to fracture of the ethmoid. Ultimate nasal obstruc-

tion, due to tumefaction of the mucous membrane, seemed to have been treated with success topically with nasal, intranasal, and ethmoidal douches of salt water.

Bone Cyst of the Ethmoid Cells.—Thompson (*The Laryngoscope*, March, 1911) reports a case of a lady who had been annoyed for several months by a very profuse serous discharge from the right nostril when she stooped. This discharge was found to escape from a small opening in the top of carious bone in the wall of the bulla ethmoidalis. The dividing walls of the ethmoid cells had all been destroyed, making one cavity of the lateral mass of the ethmoid bone. This cavity was lined by a thin, white, glistening membrane, the typical cyst lining in appearance. This membrane was curetted lightly, the cavity was packed for twenty-four hours to control hemorrhage, and then removed. A month later it was reported that the only change was that the discharge was now continuous, whereas formerly it had taken place only upon stooping. Inspection of the nose showed a free opening into the cyst with fully two-thirds of the cavity covered with normal membrane. Six weeks later the patient reported entirely well.

Ulceromembranous Laryngitis.—Moure (*Revue Hebd. de Lar., d'Otol. et de Rhinol.*, March 11, 1911) reports and discusses 3 cases, 1 of Reiche, 1 of Arbow Smith, and 1 of his own, in which he identified the affection with the pathological features of Vincent's angina.

Calcined Magnesia in the Treatment of Diffuse Papillomas in the Infant Larynx.—Claoué (*Annales des Mal. de l'Oreille, du Lar., du Nez et du Pharynx*, Livraison 1, 1911) reports two cases of his own and refers to a third in the practice of a friend in which diffuse recurrent papillomas of the larynx, after operation, underwent retrogression under treatment of one-half gram of calcined magnesia daily for a few weeks. He mentions that in veterinary medicine papillomas are very frequent, especially in the mouths of dogs, and the heroic, while empiric remedy is calcined magnesia. (Small doses, three grains each, of sulphate of magnesia have been known to produce similar results.)

Acute Thyroidism following Removal of Thyrolingual Cyst.—Davis (*Journal of Laryngology, Rhinology, and Otology*, January, 1911) reports this case. A girl, aged seven years, had a small swelling under the jaw in the middle line which the parents wished removed, as it was a disfigurement. A cyst as large as a grape was found attached to the tongue and hyoid bone, from which it was easily removed entire, the wound sutured with horsehair and closed with collodion. The child became restless in the evening, the temperature rising to 104°, with intermittent and irregular pulse (160 per minute), dilated pupils, and intense facial congestion—signs of acute thyroidism. The neck became swollen and puffy, and continued so for six weeks. The wound healed by first intention. The child complained of no inconvenience beyond "her heart thumping." The disturbance was attributed to leakage of thyroid secretion and its absorption in a wound which was undrained.

Pharyngoscope.—André (*Annales des Mal. de l'Oreille, du Lar., du Nez, et du Pharynx*, March, 1911) describes a new pharyngoscope very much on the model of Hays', but provided with an articulating mirror which can be deflected in different directions by a guide in the handle.

Embryonic Cysts of the Gums and Retropharyngeal Region.—Onodi exhibited to the Royal Hungarian Society of Physicians (*Jour. of Lar., Rhinol., and Otol.*, August, 1911) an eight months' fetus with cysts in the gums and retropharynx filled with embryonic jelly. The retropharyngeal cyst was 10 mm. long, 13 mm. high, and 16 mm. broad.

Telangiectasis Affecting the Mouth, Pharynx, and Larynx.—Safranek reports (*Jour. of Lar., Rhinol., and Otol.*, August, 1911) this case in a male patient, aged twenty-six years. The right half of the face showed dilated veins, and in the lateral region of the neck the veins showed through the skin as distinct bluish streaks. On the undersurface of the tongue the veins were enlarged to the thickness of a quill. On the dorsum near the tip the dilated vessels had formed two blood-spaces about the size of a bean. On the right side of the soft palate a network of dilated vessels was visible. On the alveolar process of the lower jaw there was a purplish swelling about the size of a bean, composed of tortuous vessels and a similar, but larger tumor lay in the recess of the right pyriform sinus. No further changes were discoverable in the circulatory or other organs.

Lipoma of the Pharynx.—Kenyon reports (*Jour. Amer. Med. Assoc.*, June 17, 1911) a large lipoma of the laryngopharynx removed extraorally under cocaine from a woman aged twenty-seven years. It measured $3\frac{1}{4}$ inches in length, $2\frac{1}{4}$ inches in breadth, and 1 inch in thickness. The patient did well, and three years later reported with an increase of weight from 124 to 156 pounds. The pharynx appeared normal except for two or three small obscure patches of thin, shiny, scar tissue.

Malignant Rhinomaxillary Myxoma.—Botey reports (*Annales des Mal. de l'Oreille, du Lar., du Nez, et du Pharynx*, 1911 No. 6,) a case of this kind, with fronto-orbital and meningeal propagation recurring after extensive exenceneration, and terminating fatally with symptoms of meningo-encephalitis some two and one-half months after the intervention. The reporter refers to a number of instances of malignant pure myxoma in other regions of the body which recurred almost inevitably after operation. The case referred to is unique in its position and extent. The only case resembling it which he could find was a pedunculated myxoma of the nasal septum, removed by Chiari, with cure of the patient.

Foreign Bodies in the Esophagus.—Guisez, in an elaborate article based upon his most recent cases of foreign bodies in the esophagus and tracheobronchial tract, describes (*Annales des Mal. de l'Oreille, du Lar., du Nez, et du Pharynx*, March, 1911), among others, two very ingenious instruments—one for cracking bones which are impacted in the walls of the tubes, and a tube capable of dilatation at its distal extremity, so as to stretch the walls of the esophagus and facilitate the better grasping of the foreign body.

OTOLOGY.

UNDER THE CHARGE OF

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The Treatment of Syphilis by Means of Ehrlich's Arsenobenzol.—Finger, Kren, and Alexander (*Wien. klin. Woch.*, 1910, No. 47, 48, and 50). The first of these papers is a summary of 170 carefully observed cases subjected to this treatment during a period of five months, in the author's clinic, the observations being further continued after the termination of clinical attendance. The importance of the observations made, in the general aspect of the subject, entitle the communication to careful reading, but for the purposes of a special review it may be excerpted with advantage. A patient, aged twenty-two years, with tertiary syphilis, exhibited, on the first day after the injection, nystagmus, dizziness, and typical vertigo of direction, the auditory apparatus remaining intact. These isolated implications of the vestibular nerve disappeared in a few days. The second case was that of a patient, aged twenty-five years, with an acquired syphilis of six weeks' duration, who, nine weeks after the injection, became the subject of a binaural labyrinthine impairment of hearing which had continued unchanged at the time of the last observation, three weeks after its onset. The Wassermann reaction was negative. The third case was that of a patient with syphilis of three months' standing, who became the subject of labyrinthine impairment of hearing three months after the injection, a condition which had remained unchanged during a period of three weeks' careful observation; in this case, also, the Wassermann was negative. In the first of these cases it was the opinion of Ehrlich that the evidences were those of the Herxheimer reaction, the vestibular nerve being the seat of a latent syphilitic affection, which, exacerbated under the influence of the injection, resulted in swelling and corresponding pressure upon the vestibular nerve. To the two latter cases, however, this explanation is not applicable, in both of them the Wassermann was negative, there had been no secondary manifestations, nor were these justly expected, and the aural symptoms would, inferentially, be referable to the arsenobenzol as their cause. The observations of Kren, reported in the following number of the same publication, covered 140 cases subjected to this form of treatment. The existent aural complications in the observed cases were of a simple character, catarrhal conditions of the tympanopharyngeal tube, middle-ear disturbances, and occlusion of the external canal. One patient, aged thirty-four years, exhibited, two months after an injection of 0.5 arsenobenzol, a labyrinthine deafness; in this case, observation in the clinic of Urbantschitsch left the question still open as to the responsibility of the constitutional disease or of the medication for the aural condition. In 60 cases treated with arsenobenzol and referred to the Urbantschitsch clinic by Riehl, Finger, and Ehr-

mann, 5 cases of monaural implication of the vestibular nerve were observed, the symptoms including dizziness, vertigo, and vomiting, a rotary nystagmus toward the sound side, with absence of caloric or rotation nystagmus; the evidences of vestibular implication began three hours, five hours, and three days after the injection. In 9 cases of aural implication in recent syphilis observed by Alexander, the disturbance of hearing occurred, in 1 case in the thirteenth week, and in the others not until the fourth month; in no instance was the implication so serious as in the cases reported by Finger, and the author is of the opinion, supported by the literature of the subject, that acute luetic neuritis is rare in the early stages of the disease. Of 270 cases observed by Riehl, there was but one in which the administration of arsenobenzol was followed by evidence of implication of the auditory nerve and these symptoms were transitory.

Otosclerosis.—Emil Froeschels (*Zentralbl. f. Ohrenheilkunde*, Band ix, Heft 6). In a review of the contributions to the study of this subject, published within the last two years, since the communication of Heimann (*Monatsschr. f. Ohrenheilkunde*, 1909), in which the characteristic symptoms of this disorder were defined and grouped, Froeschels urges the importance of continued observation and investigation into a subject which is commanding universal interest among otologists. The otosclerosis usually begins during adolescence, and is more common in women than in men, and progresses with increasing impairment of hearing accompanied by annoying subjective tinnitus, and occurs, in the great majority of cases, in both ears but not simultaneously. In the typical form of the disease the drumhead exhibits no indication of catarrhal condition of the tympanopharyngeal tube and tympanum, nor evidence of adhesive process in the middle ear; not infrequently there is a roseate glow in the lower portion of the drumhead referable to injection of bloodvessels on the promontory. In the early stage of the disease the tuning-fork tests indicate plainly the obstruction to sound transmission in the middle-ear sound transmitting apparatus, in the later stage the duration of hearing of the tuning fork by bone conduction is shortened and the hearing for high tones decreased, symptoms indicative of the secondary labyrinth implication; in this stage, also, dizziness is a not infrequent symptom, and occasionally vertigo, severe and of sudden onset. The principal localized abnormality is the bony ankylosis of the stapes and, in the majority of cases, osseous newgrowth on the promontory, and, according to some observers, some other portions of the petrous process. Habermann regards the tympanic mucosa as the starting point of the proliferous process, but Politzer, Siebemann, and many others hold that in the typical otosclerosis the tympanic mucosa is uniformly normal. Under favorable hygienic conditions the otosclerosis often remains stationary for considerable periods, growing rapidly worse, however, under the influence of excessive demands upon the nervous strength, as, for instance, during gestation. The disease is one but little amenable to treatment except in so far as general hygiene and moderate mobilization and moderate stimulation of the intratympanic circulation are concerned. The paracusis willisii, which is not an infrequent accompaniment of this disorder, as of other disturbances in which stapes

ankylosis is an important factor, is explained by Urbantschitsch on the basis of an increased excitation of the auditory nerve, and by Politzer under the more tenable hypothesis of the increase in mobility of the stapes, and other portions of the sound-transmitting apparatus under the influence of the larger sound waves. The etiology of the disease is as yet undetermined. Among French authorities the distinction between the catarrhal processes in the middle ear and the changes characteristic of the disease in question is not clearly marked. Politzer, Siebemann, and some others regard it as a disease entirely independent, in its origin, of the tympanic mucosa, but originating in the labyrinth capsule itself with later implication of the tympanic contents. That heredity is an important factor has been noted by many observers, and especially by Hammerschlagg (*Monatsschr. f. Orhenheilkunde*, 1910, p. 709), who gives the report of families in which congenital deafness and otosclerosis were repeatedly exhibited. The discovery of the Wassermann reaction led to a series of investigations as to the possible relationship between otosclerosis and syphilis, but the sufficiently extensive investigation of Busch, Zange, Arzt, and Oscar Beck in regard to this matter have definitely pronounced against any such causative relationship.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Bactericidal Effect of Blood upon Pneumococci.—Dold (*Arb. a. d. Kais. Gesundh.*, April, 1911) presents his observations on the effect of serum and blood on the pneumococcus. The blood serum of the laboratory animal is known to have no bactericidal effect on pneumococcus, but it had recently been found that human blood was actively bactericidal *in vitro*. Dold finds bactericidal substances varying in amount at different times, and highest in febrile patients. The whole blood apparently is superior by far to the serum in bactericidal powers, and these qualities are not destroyed by heat. The blood of laboratory animals fails to show these positive results, which fact is probably merely an indication of the susceptibility of different species to the pneumococcus. The bactericidal substance is probably existant as a lucein in the leukocytes, and is not secreted by them during their life.

The Permanence of Atypical Characters of Bacillus Coli.—Cecil Revis (*Centralbl. f. Bakteriologie, etc.*, Band xxxi, No. 14) cites a strange observation with regard to changes undergone by Bacillus coli under partial inhibition by malachite green. With weak solutions a number of forms of Bacillus coli were almost entirely inhibited, but one grew

very luxuriantly, and, after a number of subcultivations, it lost the power to produce gas, while it preserved its characteristics otherwise. This loss of power of gas production has existed to the present after a sufficient number of cultivations have been made, and there is no indication of any loss of vitality in other ways. Characters so acquired are generally relinquished by bacteria in a comparatively small number of generations, but this strain of Bacillus coli seems peculiarly tenacious of its acquirement.

Bacteria and the Intestinal Wall.—An interesting series of experiments has been carried out by M. B. Ravenel and B. W. Hammer (*Journal of Medical Research*, June, 1911), with a view to determining whether or not Bacillus prodigiosus could be passed through the intestinal wall and appear in the blood after injection into the rectum. In a series of a dozen rabbits, carefully tended to prevent them from nullifying the results, the findings were remarkably uniform, and in no case were Ravenel and Hammer able to find bacteria in the blood at periods varying from one and one-half hours to five and one-third hours. They did not find either that the organisms were carried far by antiperistalsis, for the bacteria injected into the rectum did not ordinarily reach the bowel above the ileocecal valve. In some cases five hours were sufficient to allow the disappearance of the organism from the rectum; and, however much one may feel convinced to the contrary, the observations of Ravenel and Hammer indicate that there is evidently no passage of large numbers of bacteria into the circulating blood.

Do Infected Cattle Necessarily Eliminate Tubercle Bacilli?—In the *Journal of Medical Research* (June, 1911), Varanus A. Moore reports four years' work upon the elimination of bacteria in cattle known to be tuberculous, as well as in those which have merely given a tuberculin reaction. His observations show support of the old view, that tubercle bacilli are not ordinarily present in the milk of animals which show no symptoms, even though they react; he finds further that tuberculous disease of the udder is very certain to show itself by the presence of bacteria in the milk, and further, that the milk is accidentally infected in those cases in which cows have open lesions almost without regard to whether these lesions are in the respiratory, the reproductive, or the digestive tract. Moore experienced some difficulty by reason of frequently finding acid-fast bacteria, which proved non-productive of tuberculosis in the guinea-pig.

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ORIGINAL ARTICLES

A STUDY OF THE MYOCARDIAL CHANGES IN TWO HUNDRED AND EIGHTY-SEVEN CASES OF ENDOCARDITIS.

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It has long been recognized that prognosis in endocarditis, either of the acute or chronic variety rests primarily not on the valve diseased nor even to a very marked grade on the degree of the valvular lesion, but chiefly on the condition of the heart muscle.

Diagnosis depends mostly on the valve involved and on the nature of the endocarditis, but prognosis on the degree and character of the associated muscle change. One may also say that exact diagnosis in endocarditis is usually relatively easy, but accurate prognosis is difficult and often impossible, since it is as yet impractical to determine or to estimate the real condition of the heart muscle by our present unsatisfactory methods. The valve lesion in aortic disease for example determines the characteristic and easily recognizable physical signs of auscultation, percussion and pulse; but the tension, rhythm, and the maintenance of the circulation rest on the muscular capability and its reconstructive or latent power, factors difficult or impossible of determination.

Treatment is also mostly based on recognition of the dominance of the muscle factor and in nearly all, except possibly syphilitic cases, it is without effect on the valvular change proper, but is

directed to the heart muscle and then yields rich reward in the way of successful management of these cardiac cases. Conservation of the muscle and the correct appreciation and control of its more or less limited possibilities in endocarditis is the only line along which successful treatment is to be expected. In spite of this well attested and entirely obvious fact, one cannot but be astonished, in going over the various text-books dealing with diseases of the heart, to find how little attention is paid to the discussion of the changes present in the heart muscle in endocarditis and the manner in which they originate, notwithstanding that in all, treatment is primarily based on the tacit acceptance of the fact that the muscle condition is the most important single factor.

Among the earlier of those who fully recognized this fact, and attempted to systematically study the nature of the muscle changes in endocarditis was Romberg, whose article appeared in the *Deutsches Archiv für klinische Medizin*, for 1893. In this article, Romberg quotes largely from Koester, Stokes, Bamberger, and Oppolzer. Von Leyden, in 1896, also presented an extensive study of the myocardial changes in endocarditis with special reference to those occurring in articular rheumatism. Previous to this, Ribbert[1] conducted experiments designed to show that certain of the myocardial changes developed as the result of embolic processes occurring in the arterioles of the myocardium. Zeigler also shortly previous to this report had advanced the same idea and it remains so stated in his text-book.

On account of the great importance of this subject and because of my personal interest in it, I have made a detailed study of the types of myocardial disease which I have found associated with endocarditis in my autopsy series. The study is based on 236 cases of chronic endocarditis, 35 of acute endocarditis, and 16 of associated acute and chronic endocarditis. These cases were taken consecutively as they appeared in my post-mortem service and unfortunately have not all been studied microscopically, although all instances of questionable or of presumably unusual type have been thus observed. I have further attempted by a preliminary morphological study of the nature of these changes to thoroughly familiarize myself with the condition so that the gross diagnosis has probably in most cases been fairly correct and accurate. As the study has been upon post-mortem findings, no attempt at distinction between obstructive and incompetent valve lesions has been attempted, for the reason that I have found from my associated clinical and postmortem observations that physiological incompetence is often or usually not to be demonstrated at autopsy, being generally due, as Romberg states, to muscular rather than valve defects.

[1] Ueber experimentelle Myokarditis und Endokarditis, Forts. d. Med., 1886, vol. iv.

At the very outset it became apparent that, as Adami and Nicholls[2] state, the heart muscle changes are not usually primarily nor even secondarily dependent upon the endocardial disease. This is especially true of those instances in which a dominant toxic factor was present. In numerous cases the myocardial changes have been concomitantly caused by the very same elements which were concerned in the production of the endocarditis.

Thus, 13 instances of associated endocardial and myocardial disease occurred in general simple infections, 14, in syphilis, 16 in tuberculosis, 1 in mixed infection following typhoid fever, and 1 in epidemic cerebrospinal meningitis. By far the larger number, however, appear to have originated in those general conditions in which a reduction of general body resistance probably first produced the myocardial disease and, perhaps, favored secondarily endocardial changes, as for example, in 61 cases of nephritis, 9 of neoplasm, 4 of grave anemia, 3 of diabetes, and in 56 instances of alcoholism. In regard to the connections between alcoholism and myocardial disease associated with endocarditis, I wish to state as I have done before, that I fully agree with Cabot that alcohol does not *per se* induce cardiac disease, but I am convinced that the associated conditions which go to make up the composite picture of alcoholism do.

The ways in which the heart muscle may become involved in endocarditis may, perhaps, be satisfactorily summarized under the following chief heads.

1. It may become diseased as a common result, of the process or condition under which the endocarditis itself develops. For example, the acute parenchymatous degeneration of the heart muscle, which is the most frequent myocardial change developing in cases of rheumatic fever, doubtless arises from the same toxic cause, be it bacterial or otherwise, which determines the inflammatory process of the valve surfaces. Undoubtedly under this heading are comprised the most frequent lesions of the heart muscle associated with endocarditis.

2. It may result from the embolic plugging of one of the coronary vessels from the dislodgment of necrotic material from the diseased valve, from embolism by lodgment of the bacteria circulating within the blood stream which may have caused the endocarditis or from hyaline thrombi. As a result an ischemia or infarction of the heart muscle follows, succeeded by necrosis and usually after a few days by cardiac rupture, or if an active fibrosis occurs in the diseased area a cicatricial scar or aneurism may follow. This method of origin of muscle disease has been abundantly confirmed by the researches of Zeigler, Romberg and Ribbert, and was found present in 5 cases of my series.

[2] Principles of Pathology, vol. ii.

3. The muscle may become involved as a result of ischemia following obstruction at the opening of the coronary vessels or in the course of their lumen. Obviously this form of heart muscle change is most frequent in aortic disease and as stated by Osler may also follow from a deficient aortic pressure quite independent of coronary disease. No instances of this last character were observed, nor were any seen of obstruction of the coronary vessels without arteriosclerosis. Eight instances definitely due to coronary arteriosclerosis were found, however, nearly all occurring in aortic disease.

4. It may become diseased by the direct extension of the ulceration from the point of valve disease into the myocardium. Ulcerative and fibrotic invasion of the bundle of His in this manner has been of late frequently reported and the condition has been especially studied by Monckeberger.[3] No recognized cases of this character are included in this series, although at present, I have two probable cases of this nature under observation.

5. Myocardial degeneration or inflammation either acute or chronic may be directly set up as a result of a superjacent endocarditis. This develops most certainly in cases of mural endocarditis, although it may also occur in simple valvular lesions and invasion of the papillary muscles is especially likely to take place in such instances. Involvement of the papillary muscles is extremely frequent especially in the chronic cases, and is often largely responsible for valve incompetence. Definite mural endocarditis with myocardial disease was found in but one case of my list.

6. Involvement and fibrosis of the muscle may readily originate in the papillary muscles whose integrity has been first compromised by the overstretching which follows cardiac incompetence or relaxation of the valve rings. This may be followed by a more or less generalized fibrosis extending out from these foci, a condition which I have frequently observed.

7. Disease and especially fibrosis of the auricles undoubtedly follows the auricular distention dependent on ventricular irregularities due to disturbed muscular conductivity and arrhythmia.

8. Banti, according to Adami, has shown that venous stasis, such as occurs very commonly in various diseases of the heart including valve lesions, may, in itself produce changes in the muscle bands which become of grave import. I have never definitely recognized this process.

9. Probably most frequent of all is disease of the myocardium, notably that of the ventricles, which occurs from other causes entirely independent of the endocarditis. This was definitely the case in 81 of the 176 instances of associated endocarditis and myocardial disease in my 187 cases of endocarditis.

[3] Untersuchungen über das Atrio-ventricular bundle im Menschlichen Hertzen, Jena, Fischer, 1908.

10. There can be no doubt but that other cases occur in which the myocardial lesions are definitely dependent on the primary endocardial disease, these instances, are, however, from their varied nature, difficult or impossible of definite post-mortem recognition.

As to the character of the valvular lesions found in the group of 287 cases, I was much surprised to find that an association of aortic and mitral endocarditis was by all means the most frequent. This combination was found in 152 cases, nearly three times as frequent as pure aortic disease and over six times as common as pure mitral lesions. This is not in accord with statistics published by most other observers. Osler gives in a series of 209 cases, aortic and mitral, 41; aortic alone, 53; mitral alone, 77; tricuspid, 19; pulmonary, 15; heart walls, 33. My list further gives: 40 instances of chronic aortic lesions, 10 of acute and 2 of acute on chronic; 12 of chronic mitral lesions, 6 of acute and 4 of acute on chronic; 6 associated lesions of the aortic, mitral and tricuspid; 5 of aortic, mitral and pulmonary lesions, all except one of the chronic variety. In only 1 chronic instance were all the valves involved. The aortic and tricuspid were involved together in 3 chronic cases. The pulmonary and aortic valves were involved in 3 chronic, but no acute cases, and the mitral and tricuspid in a single instance each, in the chronic, acute and acute on chronic lists. The pulmonary valve alone was diseased in 3 chronic cases. The tricuspid alone was involved in 1 chronic and 2 acute cases. In but 1 acute instance was a mural endocarditis without a valve lesion present, although in many instances mural changes of an inflammatory and degenerative character were demonstrable in all forms of valvular endocarditis.

From all the various ways by which the muscle becomes diseased, the number of distinct anatomical changes which result are relatively few. By far the most abundant numerically as well as important physiologically, are changes of a degenerative type, which, although they are quite frequently classified as inflammatory and included under the heading of myocarditis, are really degenerative in their nature. In the entire series of 278 cases, true inflammatory change in the heart muscle was found in but 6 instances, exclusive of those cases showing fibrosis which obviously may be either degenerative or inflammatory in origin. On the other hand, muscle changes of a definitely degenerative character were found in a total of 150 instances, exclusive of those showing purely fibrotic alterations.

As was to be expected and in full accord with well established clinical observation, concerning the relative innocence of mitral endocarditis, the rate of occurrence of disease of the muscle in mitral lesions stood last of all. Among the chronic cases of mitral disease in but 5 out of the total of 12 was muscle disease of serious nature demonstrable. In 4 of these cases only was the change suffi-

cient to permit the cardiac lesions being justly classified as among the chief causes of death. This point indicates an apparent interdependence between the degree of muscle disease, or the absence of it, in determining prognosis.

In sharp comparison to mitral disease are the 52 instances of aortic lesions, 18 of which died as a direct result of the cardiac disease and in all except 15, of both cardiac fatal and non-fatal cases, definite muscular changes were present. In all the 10 instances of acute aortic lesions the heart muscle was grossly diseased, and the cardiac lesion was rated as among the chief causes of dissolution. This indicates what has long been recognized, namely, that aortic lesions are usually the most serious of those of the endocardium. The high percentage of muscular involvement in aortic endocarditis is probably partly due to the greater mechanical muscle strain present in this disease.

In cases of associated chronic aortic and mitral disease but 22 of the 128 died as a result of the cardiac disease; yet in these same instances, the muscle was definitely and grossly diseased in all but 35 instances. Of the 15 acute associations of aortic and mitral lesions, the heart muscle was gravely involved in all except 5 instances.

As to the relationship between the valve lesion and the type of muscular change, I find that in associated aortic and mitral lesions 36 cases show purely fatty changes, 9 fatty and parenchymatous and 15 purely parenchymatous; 17 showed interstitial changes. In but a single instance was a simple muscular hypertrophy without degenerative alteration present. In the group of pure mitral disease, the number of cases was too small, only 5 out of 12, to permit conclusions of any definite value to be drawn, but here again, fatty degeneration led with 3 out of the 5 cases.

It was confidently expected that at least some examples of pure simple hypertrophy would be found in the group of chronic aortic disease, but on the contrary, as before stated, the highest percentage of muscle disease was found in this list. Death from cardiac lesions was also more frequent in these than in any other series of cases. Six instances of fatty degeneration were found, 6 of pure parenchymatous, 2 of fatty degeneration and brown atrophy, and 5 of brown atrophy alone. But a single instance of purely fibrotic change was present, but interstitial alterations were associated with fatty degeneration in 2 instances and with brown atrophy in 1. In the acute cases of aortic disease simple hypertrophy was present once, parenchymatous degeneration, twice; parenchymatous and fatty, once; fatty, once; brown atrophy and fatty, once; interstitial, twice; and inflammatory or true myocarditis once.

In the entire group of chronic cases pure parenchymatous changes occurred but twenty-five times, while fatty changes were present in 67 instances, associated fatty and parenchymatous in 17. I

was somewhat surprised at finding in the entire series of chronic cases only 22 instances of pure interstitial change, 17 of which, as before stated, occurred among the associated mitral and aortic lesions.

From this series, it appears that the most frequent myocardial lesions occurring with endocarditis are degenerative in character. Of these, fatty degeneration is the most frequent. In this general study no attempt has been made to present unusual and rare conditions, such as hyaline and amyloid degeneration but the object has been to obtain a general idea only of the most frequent changes to be expected in the heart muscle in the course of endocarditis.

It is, therefore, unnecessary in this place to go into a discussion of the various types of myocardial degeneration or to elaborately describe the changes present in them. For our purposes, it is, perhaps, sufficient to point out that fatty degeneration occurs in most cases as a sequence of an unhealed parenchymatous degeneration and parenchymatous degeneration of greater or lesser grade is present in the heart muscle in practically every instance of toxic disease, unhealed cases of which then pass over into the fatty change. Munk[4] has shown that myaline and protagen are formed in fatty degeneration of the heart muscle just as in other types of this degeneration elsewhere, so that in all probability the change is precisely like that occurring in voluntary muscle. This work has been verified by A. Erlandsen. Monckeberg found fatty degeneration of the atrioventricular bundle and according to him this type of degeneration is apt to be succeeded by calcification and fibrosis. It is, therefore, highly probable that fibrosis occurs usually as a sequence of a preliminary fatty degeneration which would account for the frequent association of these changes.

Conclusions. Myocardial disease is present in greater or less degree in practically all cases of endocarditis acute or chronic.

The type and degree of these changes determine to a large degree, the possibilities and the future of any case of endocarditis.

The most frequent changes in the myocardium in association with endocarditis are degenerative ones. Inflammatory lesions are relatively rare.

In most instances the myocardial change is not determined by, nor is it the direct result of the endocarditis, but is caused independently by the same, affiliated, or by entirely independent conditions.

The most frequent form seen in chronic or late acute cases is fatty degeneration, a lesion which differs in no material histo-chemical respect from that involving voluntary muscle. From analogy, it seems that this degeneration in most instances succeeds a primary parenchymatous alteration. As a sequence to fatty degeneration, fibrous replacement and probably brown atrophy frequently appear.

[4] Diss., Berlin, 1907.

There is no regular association between the special valve lesion and the type of associated myocardial degeneration, except that these changes appear more constantly and in most serious grade in aortic than with other lesions, probably because of mechanical reasons.

REPORT OF A CASE DEMONSTRATING PULSUS ALTERNANS, BLOCKED AURICULAR EXTRASYSTOLES, AND ABERRANT VENTRICULAR ELECTRIC COMPLEXES.

By Leo Brooks Rosenthal, M.D.,
NEW YORK.

The following case is of interest because of the presence of alternation in the pulse, the occurrence of blocked auricular extrasystoles and an aberrant type of ventricular complex in the electric curves.

History. J. H., aged forty-five years, a widower, is employed as a butler. He was admitted to University College Hospital, London, on April 1, 1911. His father is aged seventy-six years; hale and hearty. His mother died of nephritis, aged sixty years. One brother died of rheumatic fever, aged thirty-five years, another of diabetes, aged twenty-eight years, and a third, of cirrhosis of the liver, aged forty-two years. A sister died in early life of a disease unknown to the patient. Three brothers and a sister are still living and well. As a child the patient had measles; later, at the age of eight years, diphtheria. Scarlet fever, chorea, rheumatic fever and tonsillitis are denied.

When aged twenty-five years, the patient suffered from an atypical attack of pneumonia. Its duration was ten days; the fever declined by lysis and convalescence was prolonged. Ten years later the patient had an attack of severe pain in both calves. There was no fever and no joint involvement. This attack lasted eight days and he remained in bed three days. He has had repeated attacks of "influenza." The first occurred at the age of twenty-four years, the second when aged forty-one years, and the third and last attack occurred twenty months ago. Each attack lasted approximately ten days. No complications are known to have followed the first two of these attacks.

All of the symptoms relative to the patient's present condition date from the last attack. Immediately after it he experienced dyspnea on exertion, mild but persistent cough and general weakness. Attacks of palpitation were apt to occur after exertion, excitement, or gastronomic indulgences. His general health remained fair, however, and he was able to pursue his work until some months

ago, when his symptoms became exaggerated, persistent dyspnea being the most distressing symptom. Pain was never present.

Up to two months ago the patient was a moderate drinker and smoker—one or two glasses of ale per week and three pipes daily. Since the onset of this attack he has neither drunk nor smoked. Patient denies all venereal infection. No history of syphilitic manifestations is obtainable. Bowels regular; appetite good; sleep fair.

State on Admission. The patient is a fairly well-nourished man. The mucous membranes are cyanotic. There is considerable dyspnea. The thorax is markedly rachitic.

Respiratory System. The lung-liver border in front is at the sixth rib. The lower limit of the lungs posteriorly is at the tenth thoracic vertebra. The borders alter little with respiration. The percussion note is clear over the whole chest. On auscultation, numerous sibilant and sonorous rales are heard. Over a circumscribed area 4 cm. in diameter, and situated in the third and fourth intercostal space in the midclavicular line of the right chest, numerous fine crepitations are audible. Expiration is universally prolonged.

Cardiovascular System. All palpable vessels are soft. The pulse is markedly irregular; its rate per minute is 85 to 100. The systolic blood pressure is 150 mm. Hg. The apex beat is felt in the fifth intercostal space in the midclavicular line, and is diffuse and wavy. There is no thrill. The right limit of cardiac dulness lies 4 cm., the left limit 11 cm. from the mid-sternal line. Upper limit of cardiac dulness is at the third rib. There is marked epigastric pulsation. The sounds at the apex are dull and distant. A soft systolic murmur is present. The second aortic sound is accentuated.

Abdomen. Liver, spleen, and kidneys are not palpable. No ascites present.

Extremities. There is slight edema of the lower extremities.

Nervous System. Negative.

Urine. Acid; traces of albumin; no sugar. In the sediment there are occasional granular casts, a few white blood corpuscles and amorphous urates.

Sputum. The sputum was negative for tubercle bacilli on three successive occasions.

During his stay in the hospital the patient's pulse became more regular. The systolic murmur disappeared. The edema cleared up, and the breath sounds became free of rales and crepitations. The blood pressure fell to 100 to 110 mm. Hg and stayed there. All subjective symptoms were markedly relieved.

The Polygraphic Tracings. The pulsus alternans is well shown in the accompanying tracings (Figs. 1 and 2). As is usual, when pulse alternation is combined with extrasystoles, the alternation is more marked after the premature beat. It may be noted that, as

pointed out by Windle,[1] the alternation sometimes becomes more prominent before the advent of the extrasystole (Fig. 2). The phase of respiration in which the extrasystole occurs, seems to bear no fixed and regular relationship to the degree of alternation. This relationship was present in certain of Windle's cases.

The concurrence of extrasystoles with the *pulsus alternans* so confused the radial curves that at first the case was taken for one of fibrillation of the auricles.

FIG. 1

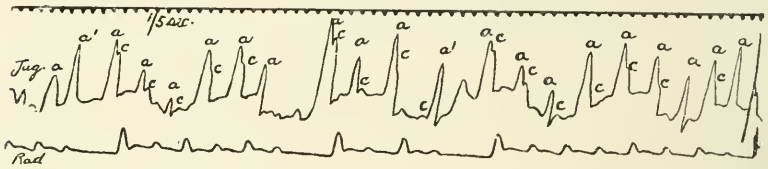
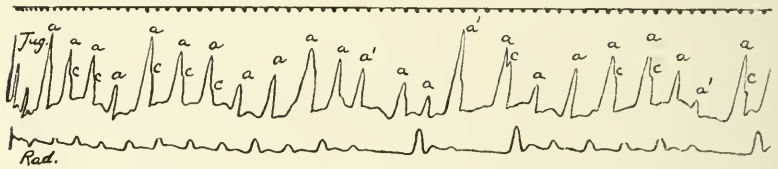


FIG. 2



FIGS. 1 and 2.—Polygraphic tracings. The radial curves show marked irregularity, as a result of auricular extrasystoles and alternation. In the jugular tracings of Figs. 1 and 2, at the points marked *a'*, peaks are seen which correspond to auricular extrasystoles. Fig. 2 shows the increase in alternation before the occurrence of the extrasystole.

The Electrocardiographic Curves. A large number of electrocardiographic curves have been taken from this patient, many with simultaneous radial curves. They are of interest from several points of view. Characteristic extrasystoles are shown in the accompanying figures. The lead in each case was from right arm to left leg.

The rhythmic beats are represented by small *P* summits, corresponding to auricular systoles; *R*, deep *S*, and *T* summits correspond to ventricular systoles. From time to time, the regular rhythm is interrupted by premature beats readily recognized as arising in the auricle. Examples are shown in Figs. 3, 4, and 6. Taking the most simple form of mechanism, such as is shown at the end of Fig. 3, and considering the last four cycles of this figure, we have first a normal beat accompanied by the usual summits. A beat of the same character follows it, but one in which *T* is deformed by a downward directed peak (*P*), representing the ectopic and premature auricular contraction.

[1] Observations of Pulsus Alternans, Heart, vol. ii, p. 95.

This premature auricular contraction, represented by an anomalous complex in the electric curve, is followed by a ventricular complex of almost normal form for this patient. It differs from the usual complex only in so far as R is increased and S slightly diminished. The fourth cycle at the end of this figure represents the beat which follows the pause. It is of perfectly normal outline.

We have then, in the first instance, a clinical picture of a premature auricular contraction, represented in the electric curve by an anomalous auricular complex and a practically normal ventricular complex. The slight variation noticed in the ventricular complex is not an uncommon accompaniment of premature auricular beats,

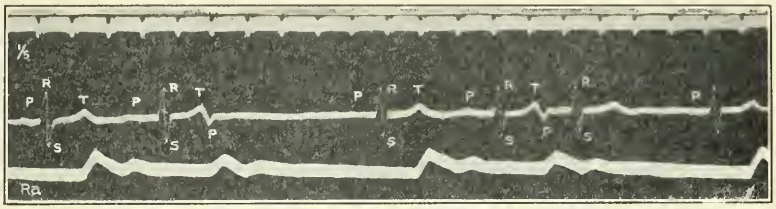


Fig. 3.—Simultaneous electrocardiographic and radial curves, showing two premature auricular contractions, the first of which gives no ventricular response. Note the small variation following the first premature auricular contraction. Similar variations are seen in Fig. 4.

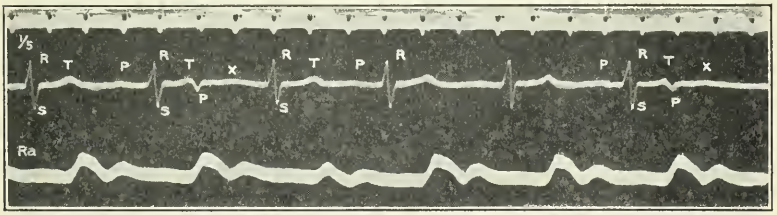


Fig. 4.—From the same case. Two premature contractions are shown. The first yields a ventricular response after an exaggerated interval; the second gives no response.

and will be further referred to in a subsequent paragraph. For the time being it may be well to notice that the P-R intervals corresponding to the premature contractions are rather larger than the P-R intervals of normal beats. But this phenomenon, the increase of the P-R interval accompanying normal cycles, is at times considerably exaggerated; a curious example is shown in Fig. 4, where the P-R interval for the first abnormal cycle is increased to $\frac{2}{5}$ seconds. The increase is so great that the corresponding ventricular complex, instead of falling prematurely, falls at the expected point. This phenomena is seen in rather an exaggerated form in the arterial curve accompanying the electrocardiogram. The radial up-stroke accompanying the abnormal cycle falls late and is small.

Further exaggeration of the *P-R* interval is not found. The next stage is marked by the presence of blocked beats. One of these is shown at the beginning of Fig. 3, another at the end of Fig. 4.

The premature auricular contraction is clearly recognized in the electric curves by the deformity it produces in the *T* wave with which it is synchronous. It is followed by no ventricular complex, but is succeeded by a summit which has hitherto received no description. If the long pause succeeding the blocked auricular contraction is carefully examined, a small and low summit marked *X* will be found, the apex of which falls at a distance of one and three-fifth seconds, after the abnormal auricular complex. This summit

Fig. 5.—From a different case. An electrocardiogram showing two premature auricular contractions, the second of which is blocked.

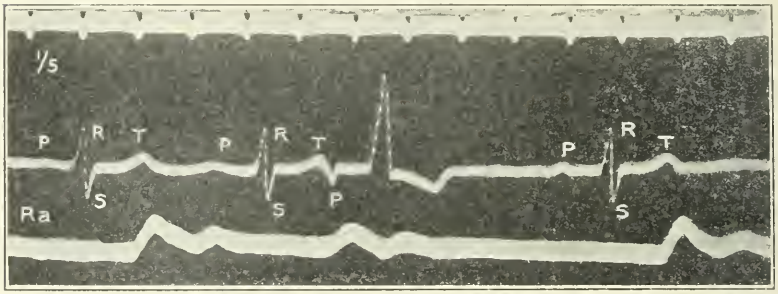


Fig. 6.—From the same case as Figs. 1 to 4. An electrocardiogram showing a single premature auricular contraction. The ventricular response is accompanied by an aberrant ventricular complex.

is found regularly after all blocked premature auricular contractions in the curves from this patient, and appears to be associated with the abnormal auricular contraction. The same wave is seen after the first premature auricular contraction of Fig. 4. It is not found in any other position in the curves.

Blocked premature auricular beats have been previously described by Hewlett[2] and Lewis.[3] A new curve is published from the patient described by the latter, and is shown in Fig. 5. This figure shows a normal cycle, of which the *T* summit is deformed by a downwardly directed peak at its opening phase. This is the rep-

[2] The Blocking of Auricular Extrasystoles, Jour. Amer. Med. Assoc., vol. xlviii, No. 19, p. 1597.
[3] Paroxysmal Tachycardia the Result of Ectopic Impulse Formation, Heart, vol. i, p. 261.

resentative of the abnormal auricular contraction. It is followed after a rather prolonged *P-R* interval by a premature ventricular complex of normal outline. The pause following this is succeeded by two normal cycles. The *T* summit of the last cycle is deformed by a premature auricular contraction, and this impulse is blocked and is followed by a long pause of four-fifths of a second.

It has been said that in the patient who forms the basis of this paper, the ventricular complexes corresponding to premature contractions arising in the auricle are usually of approximately normal outline. And it has been said that the deviations consist in a slight increase in the summits *R* as compared with normal beats. This increase is well shown in Fig. 3. At rare intervals the same patient showed a striking form of "aberrant" beat,[4] an instance of which is given in Fig. 6. There can be no question that this aberrant complex (Fig. 6) is in reality the representative of a ventricular contraction of supraventricular origin. It is another example of the phenomenon described by Lewis,[5] and it is of peculiar interest in that it shows relationships of a precisely similar nature to those described by this writer. Thus, it occurs in a case in which conduction disturbances in the junctional tissue are clearly marked and readily demonstrated. It is noteworthy that both in the original description of the phenomenon and in the case here described, blocked premature auricular contractions were present. The other point of interest is the fact that the aberrant type of response is the response which occurs soonest after the preceding ventricular contraction. Thus, comparing the two premature auricular contractions of Fig. 3 and the premature contraction of Fig. 6, the ventricular complex accompanying the former stands at a distance of two and two-fifths seconds from the preceding ventricular complex, while the aberrant complex of Fig. 6 stands at a distance of two-fifths seconds from the preceding auricular contraction. Thus, aberration appears when the pause preceding the beat in which it is shown is shortest and when the rest is shortest.

The interpretation which has been adopted in explanation of these phenomena of aberration is confirmed by the present findings. The patient now recorded presents aberrant complexes, and these aberrant complexes are closely associated with conduction changes in the junctional tissues. Moreover, the degree of aberration is apparently dependent upon the relative lack of rest which the junctional tissues experience in an individual instance. It is upon the occurrence of these phenomena that the view is based, that the anomalous ventricular complexes are dependent upon conduction defects in individual branches of the arborization. Considering the

[4] A term which is fully explained by Lewis in "The Mechanism of the Heart Beat," London, 1911.

[5] On the Electrocardiographic Curve, etc., Heart, vol. ii, p. 23.

ventricular complexes accompanying premature contractions in this patient, it is evident that each results from a supra-ventricular impulse, an impulse which has come down through the main bundle and which has spread through the two chief divisions of the bundle and the arborization on each side. Under ordinary circumstances, impulses travelling in this manner may be expected to and do give rise to contractions of the ventricle which yield normal ventricular complexes. It is difficult to see how the deformity of the ventricular complexes in this patient is produced, unless the impulses which give rise to them have followed an abnormal course after reaching the ventricle. In the example shown in Fig. 6, the complex closely resembles a premature contraction arising in the right or basal portion of the ventricle, and it may be suggested that the main defect, in the conduction of the impulse which produces this beat, is in the left branch of the bundle or its branches. Curves of this form have been shown to arise when the left branch of the bundle is cut experimentally.[6]

The observations upon which this paper is based, were carried out in Dr. Thomas Lewis' department, at the University College Medical School, and I have to thank Dr. Lewis for permission to record this case, as well as for invaluable aid in preparing the manuscript.

ACUTE DILATATION OF THE STOMACH IN PNEUMONIA.[1]

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The purpose of this paper is to bring more prominently before the profession the fact that acute dilatation of the stomach is a real complication or sequel to pneumonia fraught with great danger to the patient, usually easily relieved and generally unrecognized.

The condition according to Laffer was first described by Rokitanski in 1842. Since that time it has been more or less before the public. Fagge described the condition accurately in 1872 in *Guys Hospital Report.* In spite of these articles written so early, it was only twelve years ago, or in 1899, when Albrecht published his article in *Archiv für Pathol. Anatomie* and collected but 19 cases. In 1907 Conner, in his article in the American Journal of the Medical Sciences, collected 102 cases. The very next year

[6] Eppinger and Rothberger. Ueber der Folgen der Durchschneidung der Tawara'schen Schenkel der Reizleitungssystem, Zeitschrift f. klin. Med., vol. lxx.

[1] Read before the Association of American Physicians, May 10, 1911.

Laffer (*Annals of Surgery*, March and April, 1908) was able to collect 217 cases, and since and including 1907, I find no less than 86 references to the subject, some of them citing new cases. By far the greatest number of cases cited are postoperative.

Practically all text-books which speak of acute dilatation of the stomach, have the stereotyped sentence that it sometimes occurs in severe acute, or wasting diseases, but I fail to find any article upon pneumonia, in any book, which speaks of this syndrome as a complication or sequel of pneumonia.

Even the elaborate and classic article by Musser and Norris in Osler's *System*, fails to speak of it. From the fact that I have met with 4 typical cases, 3 within the last year, and another of slight but severe, ileus and dilatation, forces me to believe that I, in common with others, have heretofore mistaken this condition for something else.

I detail below 5 cases of this condition which have occurred in may own practice as a complication in pneumonia, and 6 cases from the literature, making 11 cases so far reported.

Cases which have been carefully autopsied show in practically every case a constriction of the duodenum at the root of the mesentery.

The one feature which attracts attention in all of the cases which have come to autopsy, is the huge size of the stomach, often the stomach occupies the entire abdominal cavity. Sometimes the wall of the stomach is actually thickened, sometimes it is thinned. Conner's statistics are as follows:

In 14 cases the abdominal wall is described as abnormally thin; in 3 instances the wall was mentioned as thick.

One writer on the subject, who has evidently never seen a case, believes there is no such thing as acute dilatation, but that the stomach is chronically dilated and only the symptoms are acute. This is evidently an error, for cases of the operative type have had the abdomen opened and the stomach found normal. Afterward they have died of acute dilatation of the stomach, and that viscus occupied practically the entire abdominal cavity. One such case occurred to the writer.

Miss W. Operated in 1909 for gallstones for me by Dr. James Hutchinson. The stomach was in normal position and of normal size. The patient vomited small quantities of greenish-black material. The abdomen for several days was not distended, then there was a sudden distention. The true nature of the case was not recognized, and the patient died. An autopsy showed the stomach hugely dilated and reaching to the pubis. It contained two quarts of blackish-green fluid. The stomach wall was of normal thickness.

Then, too, in some of these cases of pneumonia the stomach reached its normal size after dilatation was relieved, and the patients have not had a single sign of disease since recovery.

Fagge noted the fact that in one of his postmortem cases the stomach was of enormous size, but when it was relieved of its contents, it very rapidly retracted. This was the fact in Thompson's case detailed in this paper.

So, however inexplicable it is that a viscus should dilate to several times its normal size in a few days and the stomach wall still be of normal thickness, the undoubted fact remains that this is so. I trust, however, that individuals having the opportunity, will make careful microscopic sections of the stomach wall. Here we will doubtless find the explanation.

The question as to which is primary, the duodenal constriction or the dilated stomach is still undecided. Personally I feel that these pneumonia cases show in favor of some toxic condition affecting the inervation of the stomach, causing dilatation, this dilation in itself causes by its traction, a real constriction of the duodenum, which in turn leads to filling of the stomach with the huge amount of material often foul and stinking.

Unquestionably there are some cases with chronic dilatation, which suddenly develop symptoms, and are thus classed as acute dilatation, but they are a marked minority and can scarcely ever occur where the abdomen has been opened, or the dilated stomach seen at operation.

Acute dilatation of the stomach in pneumonia was first brought acutely to my attention in July, 1910. Since that date I have seen three other undoubted cases, and I find among my personal notes, 1904, the description of a typical case, but at the time its true relation to the attack of pneumonia was not recognized.

Case I.—Mrs. B., aged seventy-six years. In the evening of October 18, 1904, the patient was suddenly seized with chill and fever and excruciating pain on breathing, and tenderness over the region of the bladder. October 19, 1904, the temperature was about 102°. Marked dulness over the lower lobe of the right lung. October 20, 1904. On this date there was dulness on the right side over the lower lobe of the lung, from the middle of the scapula to the liver. There was marked blowing over the area. Still pain and tenderness on the right side of the abdomen. The patient made a slow but uninterrupted recovery from her pneumonia, though she was extremely weak. Suddenly, on November 5, 1904, sixteen days after the initial chill, she vomited about one quart of undigested ill-smelling material. She vomited several times that day. On November 6, 1904, she had great abdominal distention, and vomited material of decidedly fecal odor. She was weak and collapsed. Distinct peristaltic waves could be seen over the region of a distended stomach. The stomach tympany extended far below the umbilicus. The patient was seen daily during this period by Dr. John H. Musser. We believed the patient had a spasm at the pyloric end of the stomach. The stomach tube was passed and 48 ounces

of foul fecal-smelling material was removed. The stomach was then washed, and 8 ounces of milk returned by the stomach tube. The washing was repeated every six hours until the afternoon of November 7, when all vomiting ceased, and after passing many pitfalls, the patient entirely recovered.

Case II.—Seen June, 1910, with Dr. Murphy, of Richmond, Philadelphia. A young man, aged twenty years, was seized with a remarkably severe attack of pneumonia. The right lung was first involved, first the lower and then the middle lobe being affected, his left lung then rapidly became involved, and finally he had apparently only his right upper lobe in use, though by that time there was some resolution of the right base. All this time in the midst of July heat of Philadelphia, the temperature of the patient was between 103° to 104°. The pulse was extremely rapid, frequently reaching 140 per minute. Resolution began at the right base and slowly progressed, the patient's temperature dropping to normal by lysis. Suddenly, three days after the temperature had been normal, without warning he vomited a large amount of creamy, sour, not fecal material. I saw him in a few hours (I had seen him almost daily before this) and found great distention over the stomach itself. The left hypochondrium and the umbilical region were protruding while the right hypcohrondrium was flat. The complete outline of the stomach could be seen, tympany reached almost to the pelvis. The patient was collapsed, his pulse running. Notwithstanding the apparent moribund condition of the patient, a stomach tube was passed, and a great amount of the same liquid removed, and the stomach washed. There was an immediate disappearance of the tumor, and the patient was much relieved. In six hours a second washing was performed and all stomach symptoms disappeared. By August he was able to go to Atlantic City. He now weighs 156 pounds, and is in perfect health.

Case III.—H. B., married, aged thirty-five years. Seen with Dr. Walter S. Hagert, of West Philadelphia.

On January 28, 1911, the patient was seized with pneumonia. On January 30, 1911, the left lower lobe was involved, and the disease remained restricted to that area of the lung. On January 31, the temperature suddenly fell to normal. It again rose to 102°, and on February 2, there were symptoms of intestinal obstruction. The abdomen was greatly distended. It was impossible to obtain a bowel movement by any means. I saw him on the evening of February 3, 1911. The abdomen was much distended. The distention, however, was epigastric, and extended two inches below the umbilicus, forming a tympanitic tumor. His pulse was rapid, but good. He had complete consolidation of the lower left lobe, which was undergoing resolution. The patient was delirious and semicomatose. There was some vomiting. A stomach tube was introduced, and a small amount of sour material obtained,

together with much gas. The epigastric tumor immediately disappeared, and the abdomen became flaccid. The next day and three successive times the stomach was again washed. Bowel movements remained sluggish, but there was no return of distention of the stomach after the fourth washing. Eserine and strychnine were administered hypodermically. The patient today is entirely well.

Case IV.—C. J., aged fifty-four years, laborer. Seen with Dr. D. D. Custer, of Manayunk. Taken ill February 25, 1911, with what was apparently influenza. He rapidly developed a consolidation, confined to the right base. March 4, there was some abdominal distention with vomiting of dark material and retention of urine and obstinate constipation. The case had the appearance of obstruction of the bowels. Suddenly, March 5, the eighth day of the disease, there was extreme abdominal pain, distention with collapse, as shown by rapid pulse, cold sweat, and temperature of 98°. The patient was seen by me on the afternoon of March 5. He had a running pulse, was collapsed, there was marked consolidation of the right lower lobe of the lung; much abdominal pain, and an epigastric tumor extending apparently to the pubis. Great quantities, about two quarts, of foul, dark-green material were washed from the stomach, with immediate relief of pain and disappearance of the abdominal distention; the bowels moving shortly after. The temperature rose to 103°, and the man died of exhaustion fifteen hours after the stomach was evacuated.

Case V.—Mrs. H., aged seventy-six years. Seen with Dr. John McCloskey, of Chestnut Hill, April 21, 1911. Had chill on April 16, 1911. Rapid complete consolidation of the entire right lung, with some consolidation at the left base. Temperature ranged from 102° to 104°. She was seriously ill, but did fairly well until the morning of April 20, when she had a sudden collapse. Her pulse became running, her respiration extremely rapid, her abdomen greatly distended. I saw her in the early morning of April 21. She was in collapse, semi-conscious, pulse 120, with great abdominal distention, more marked in the epigastrium. Gastric area apparently greatly distended, particularly to the left. The outline of the stomach could be plainly seen. There was marked peristalsis over the entire abdomen, and we believed that the peristaltic sounds in the intestines could be distinguished from those of the stomach. No succussion splash could be developed. Apparently she had great abdominal pain. She had no bowel movement for forty-eight hours. Notwithstanding the serious condition of the patient, lavage was instituted, and about a pint of foul fecal material was removed, and salt solution introduced returned clear. There was apparently not very marked dilatation of the stomach, because while the stomach tumor itself disappeared after lavage, the

general distention still remained, and this was evidently due to distention of the intestines themselves. The patient was relieved by the washing, but died about twelve hours afterward in collapse.

CASES FROM THE LITERATURE.

CASE VI.—(Reported by H. Campbell Thompson, *Lancet*, October, 1901). Female, aged twenty-four years. Attack of pneumonia, July 24, 1901. Perfectly well previously. Consolidation of lower right lung. July 27, some friction of left base. Sudden vomiting on the 27th, continued until death on the 29th. Vomitus greenish, large quantities. No effort. Postmortem: 35 fluid ounces of dark greenish fluid. Stomach immediately returned to normal size when contents taken out.

CASE VII.—(Reported by Box and Wallace, *Lancet*, 1901, vol. ii, p. 1259). Male, aged twenty-four years. Chill, May 27, 1901. Pneumonia lower lobe of left lung, May 29, 1901. No distention on the 19th. On the 30th temperature 96°. Rise to 104° at death on eleventh day of disease after profuse diarrhea. Postmortem: pneumonia. Great dilatation of the stomach, but involved duodenum. Believe distention first due to paralysis and then to incarceration at the root of the mesentery

CASE VIII.—Case reported by Herrick, *Journal of the American Medical Association*, March 31, 1906.) E. S., aged thirty-six years. Admitted to the hospital with pneumonia. The right upper and lower lobe, and the left lower lobe were involved. The case proved to be an extremely severe one of migrating pneumonia. Temperature ranged from 101° to 104°. The pulse from 115 to 130. After the patient had been in the hospital two days, she was lectured upon, a careful physical examination was made and nothing unusual noted. On the ninth day of the disease, she was looked upon as a very ill patient, but recovery was expected. At 3 P.M. of that day she vomited a large amount of dark brown fluid. At 6.30 P.M. she vomited, and at 7.15 she vomited again. In the evening she was delirious, vomited a large amount, abdomen greatly distended, but pneumonia was improved. The abdomen showed distention, and there were splashing sounds discovered. The stomach was washed out, the patient had periodical attacks of diarrhea afterward, but recovered.

CASE IX.—(Reported by Hood, *Lancet*, 1901, vol. ii, p. 1259.) Girl, aged sixteen years. Admitted to the hospital with pneumonia of severe form. She vomited on the third day. Vomitus was dark green fluid, and then dark inky color. This continued until death, twelve hours after the beginning of the vomiting. The autopsy showed the stomach very greatly dilated, together with duodenum and jejunum.

Case X.—(Reported by Lehman, *Thesis*, Leipsig, 1904, Arterior Mesenterialen Därmverschluss.) Male, aged twenty-nine years. Begun with pneumonia, October 8, 1902. Died October 16, 1902. Developed pneumonia of both lungs. On the evening of the 13th, while the pneumonia process was apparently improving, vomited yellowish brown watery fluid. The urine was dark. The abdomen was markedly distended, particularly the left hypercondrium. They attempted to pass the stomach tube and failed. On the 15th the patient went into collapse, and on the 16th died. Autopsy showed a monstrous dilatation of the stomach, together with dilatation of the duodenum, and obstruction at the mesenteric point of the duodenum.

Case XI.—(Weber, *Trans. Clinical Society*, London, 1906, vol. xxxix). Female, aged twenty-six years. Was ill with pneumonia, June 13, 1905. On observation June 15, there was consolidation of the right lung, and also pericarditis. Suddenly on June 17, much abdominal distention; no pain, no vomiting. Stomach was washed, much black greenish material obtained. Tympany did not at once disappear, but on June 20 there was no distention, and the patient entirely recovered.

ANALYSIS OF CASES OCCURRING IN PNEUMONIA.

Recovered, 5; died, 6. Dilatation occurred before the crisis 8 times, after the crises 3 times. Distention of the abdomen was present in all cases. Collapse was reported in 5 cases. Diarrhea, in 2 cases. Vomiting occurred 8 times. Pain was very severe in 1 case, and was complained of in one other case. Most of the cases were delirious, which may account for the lack of pain in most.

As Conner has pointed out, when one has met and recognized a case of acute dilatation of the stomach, he is not likely to be misled by any case which occurs. The diagnosis in postoperative cases and in cases which arise with no apparent cause is more difficult than the condition with pneumonia, though here, too, the diagnosis must remain in doubt unless the fact of a possible gastric dilatation is remembered, and a careful physical examination of the stomach is made.

The symptoms and physical signs of the condition as may be gathered from the cases cited above are: Vomiting, abdominal pain, abdominal distention (due to enlarged stomach), constipation (diarrhea in a few cases), collapse, splashing sounds, peristaltic movement over the stomach.

1. *Vomiting.* This is the most frequent symptom. It occurred in all but one of the above cases, and was present in 90 per cent. of Conner's cases from all causes. The vomiting in two instances in my series was yellowish. In two it had a fecal odor, in the remainder

it was dark greenish or blackish in appearance. The quantity is usually large, one pint or more, though rarely it is small. The act of vomiting is painless, and has much the character of that of general peritonitis. The vomitus is suddenly and violently expelled from the mouth, without effort on the part of the patient.

2. *Pain was complained of* in 42 of Conner's cases. In this series of pneumonia cases, it occurred twice. In one of my cases it was so severe that morphine was required.

3. *Abdominal distention* usually occurs quickly, is frequently severe, and is almost without exception in the epigastrium, causing a tumor in that position, but on account of the distention being due to the large stomach, and the stomach occupying an abnormal position, the whole abdomen is distended. In one of this series the outline of the greatly distended stomach could be plainly seen. This is exactly in accordance with one of Fagge's cases. This abdominal distention completely disappeared after lavage.

4. *Constipation is the rule.* In 2 of my own cases the first thought was that probably the symptoms were due to intestinal obstruction. In 2 of the pneumonia cases, however, there was diarrhea. This constipation adds color to the picture of intestinal obstruction.

5. *Collapse.* The patient is frequently almost totally collapsed. The face is pinched and anxious. The eyes are sunken. The breathing is rapid. The patient gives every indication of almost immediate dissolution.

6. *The splashing sounds.* By placing ones hands upon the lower abdomen and making a quick percussion of the portion of the abdomen, occupied by the tumor usually a splashing sound can be detected, which is so characteristic of dilatation of the stomach. Peristaltic movement of the stomach area can occasionally be seen. This has been noted in only a few instances, and is apparently not as marked in cases of acute dilatation as it is in cases of chronic dilatation.

Diagnosis. The condition must be diagnosticated from general intestinal distention not due to obstruction or peritonitis; from peritonitis due to perforation or to extension of inflammation; from intestinal obstruction; from pancreatic cyst; from uremia; from postanesthesia vomiting; and from acute hemorrhagic pancreatitis.

General abdominal distention is common in pneumonia and is more frequently than not unaccompanied by gastric dilatation; that they may occur simultaneously is, I think, proved by my Case V. In simple distention peristalsis may be heard over the entire abdomen. The outline of the stomach cannot be made out, and the stomach tube introduced will not remove the distention; frequently in these cases a rectal tube will relieve the tympany. There is no vomiting, there is often diarrhea.

General Peritonitis. Here there is the same rapid distention as in gastric dilatation, but the stomach cannot be seen outlined.

There is much more tenderness than in dilatation of the stomach, there is no splash, and above all, there is the same collapsed condition of the patient. The stomach tubes doe not dissipate the distention.

Intestinal Obstruction. Three of the cases which occurred in pneumonia, and which I myself saw, were believed to be due to intestinal obstruction, and, indeed, the picture was very like it. Abdominal pain, vomiting, in two instances almost fecal in character, great distention, and constipation. Indeed, the later view that there is always an obstruction where the mesentery crosses the duodenum, gives real reason for the likeness of the pictures. If there is a stricture high up not due to gastric dilatation, the differential diagnosis would be impossible. In intestinal obstruction, however, the distention is originally general over the entire abdomen, whereas in acute dilatation of the stomach the distention is likely to be in the epigastrium, or at least greater in that position. Sometimes a marked epigastric tumor is seen, occupying the entire epigastrium and the left hypochondrium, and also the lower epigastric region, and in rarer instances, the shape of the distended stomach can be made out through the abdominal walls. Careful passage of the stomach tube will cause the immediate disappearance of the abdominal distention where this is due to stomach dilatation.

Pancreatic Cyst. Dilatation of the stomach has been mistaken for this condition, but in cyst there is the evidence of a true mass. This mass is dull to percussion. The stomach tube will not cause its disappearance. There is no collapse in a cyst.

Uremia. The dull unconscious condition of uremia is not like the rather active delirium of dilatation of the stomach. There is no collapse. There is no distention.

Acute Hemorrhagic Pancreatitis. In this condition there is the same sudden onset, with collapse, but the distention is general and not confined to the stomach. It is easily differentiated by the stomach tube.

Prognosis. Conner gives a death rate of 72.5 per cent. in 102 cases. Laffer a death rate of 62.5 per cent. in 217 cases. Judging from the result in pneumonia cases, 6 deaths in 11 cases, 55.5 per cent., and in operative cases where the proper treatment has been instituted early, this terrific death rate is probably largely the result of the true nature of the case being unrecognized, or improper treatment (surgical) being applied.

Treatment. It would appear that acute dilatation of the stomach is one of the rare abdominal conditions in which medical men can both advise and administer the treatment to the exclusion of the surgeon. The first requisite is early diagnosis. Sudden abdominal distention occurring in the course of pneumonia must bring the thought of acute gastric dilatation at once to the practitioner's mind. Distention, collapse, increased gastric tympany, pain, vomiting, are the suspicious signs. Before the patient is

moribund, often before the diagnosis is definitely determined, and, as a diagnostic step a stomach tube must be introduced and lavage practised. If the contents of the stomach are foul and copious, or if there is much flatus, relief will be almost instantaneous, and if the dilatation occur after the crisis, recovery may be confidently expected. The lavage must be practiced as often as the distention occurs. When a patient is collapsed with running pulse, it is often feared that the passage of the stomach tube may be fatal. This is a mistake. On the contrary, the tube is easily passed and relief is marked even in most desperate cases in the midst of an attack of pneumonia. The position of the patient is of some importance. In distention of the stomach, as has been stated, there is constriction of the duodenum, under the root of the mesentery, and the collapsed small intestines are far down in the pelvis, making the mechanical obstruction still more marked. By turning the patient on the right side or on the face, this element is probably largely removed. All food and drink by the mouth must be interdicted. Strychnine and eserine hypodermically have seemed of value in 2 of my cases.

LOBAR PNEUMONIA OF MICROCOCCUS CATARRHALIS AND BACILLUS COLI COMMUNIS ORIGIN.

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This report is based upon the study of two cases of pneumonia which were observed during the winter of 1909–10 in the wards of the Second Medical Division of Bellevue Hospital. They are of interest (1) because of the atypical clinical course exhibited by each, and (2) because of the bacteriological findings.

Case I.—Lobar pneumonia, migratory in character, all lobes of the lungs being successively involved, and one of them, the left lower, being twice consolidated. Complicated by multiple arthritis and tonsillar abscess. Micrococcus catarrhalis in pure culture from sputum. Recovery.

The patient, a colored boy, aged fourteen years, was admitted to Bellevue Hospital on December 30, 1909, complaining of pain

in several large joints, sore throat, and pain in the left side of his thorax. He had been well until December 24, 1909, when his throat became sore on swallowing, and pain and tenderness, without swelling, developed in his ankles and knees. A slight cough with little expectoration also began at that time and continued until admission. Three or four days after the onset his elbows and shoulders also became painful, while his left knee somewhat improved; his right knee and ankle were unimproved. On December 29, the day before admission, he first had a rather slight pain in the region of the left nipple, which was aggravated by coughing. No history of a chill or bloody expectoration was elicited. When admitted his temperature was 102.8°; pulse, 120; and respirations, 24.

The boy had had measles, pertussis, scarlatina, and several attacks of sore throat. His tonsils were excised in 1907. He had no cough previous to this illness.

The patient was well developed and in a good state of nutrition. Both tonsils were considerably swollen and very red; there was no membrane. His heart was normal. No abnormal physical signs were observed in his lungs or pluræ. His ankles, knees, elbows, and shoulders were very tender on pressure, and movement caused severe pain, but they were not reddened or swollen.

On December 31, the day following admission to the hospital, signs of consolidation were noted over a small area at the angle of the left scapula. His cough was more frequent and he expectorated considerable clear mucus. Leukocytes numbered 40,000, polymorphonuclears constituting 86 per cent. Urine was concentrated and contained a heavy trace of albumin, but no casts. On January 3, 1910, signs of consolidation were observed over the upper lobe of his left lung; January 9, consolidation of right upper lobe; January 12, consolidation of right middle and lower lobes. Leukocytes now numbered 66,500 with 85 per cent. of polymorphonuclears. As each new lobe became involved the lobe previously affected began to resolve, so that on January 23 the left lower lobe again became consolidated after apparently having become normal. The progress of the disease is best shown in the accompanying chart (see Chart I). On January 26, herpes appeared on both lips. The sore throat continued until January 12, when after complaining of severe pain in the right side of his throat he coughed up a considerable quantity of pus which evidently came from his right tonsil, as it was later found to be lax and ragged.

The pain and tenderness in his joints also continued, and on January 17 there were well-marked signs of fluid in both knee-joints. A culture of venous blood gave no growth. On this date signs suggestive of fluid at the base of the right lung were observed and a thoracentesis was done, which gave a few drops of clear fluid, which was also sterile.

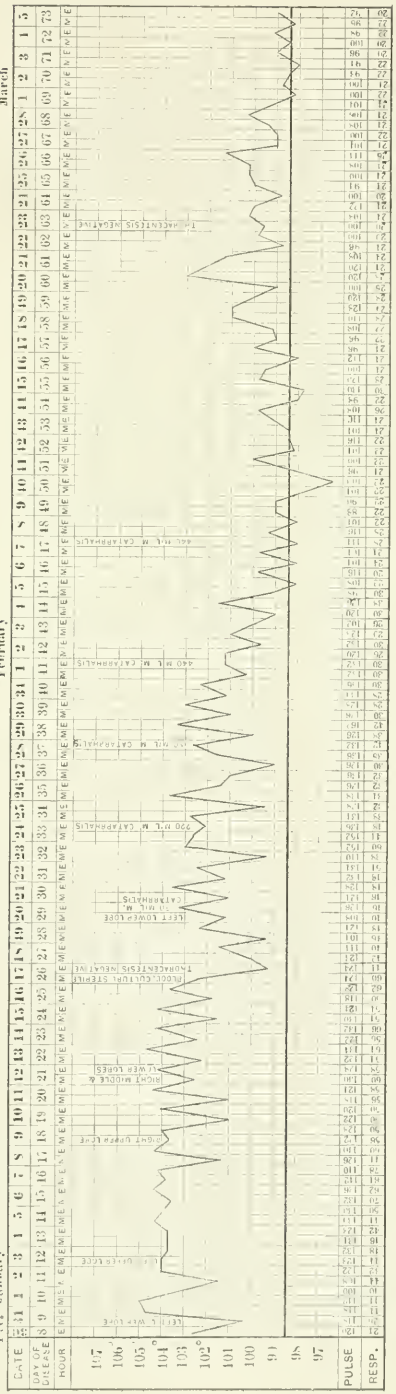

CHART I.—Migratory lobar pneumonia. Micrococcus catarrhalis in sputum.

A "clean specimen" of sputum was obtained on January 15. This consisted of rather thin, translucent, mucoid material with a few small pellets of a yellowish color. It was handled by Kitasato's method, and the culture showed a pure growth of Micrococcus catarrhalis. Two repetitions of this procedure, carried out in the next week, each time resulted in pure cultures of the same organism. A vaccine was prepared from the first culture and given in increasing doses at intervals of four days, as indicated on the chart.

During all of January the boy was very sick; his pulse became feeble and considerable stimulation was administered at different times. He was never delirious and did not appear to lose much weight. He was for some time kept in a room with all windows open and was later placed on a balcony in the open air. His diet consisted of carbohydrates and milk, and averaged 1800 calories *per diem*. Upon the appearance of fluid in his knee-joints he was given 15 grains of aspirin at four hour intervals, and the joint symptoms quickly subsided. Convalescence was rather slow, and he had some fever at times until March 1. There was an exacerbation of fever on February 19, which lasted three days, but which was unaccompanied by any change in physical signs. The patient was discharged from the hospital on March 16 and sent to a convalescent home. Examination at this time showed signs of thickened pleuræ over the posterior bases of both lungs.

The illness was evidently primarily an arthritis followed by pneumonia of a migratory character, which, together with the acute tonsillitis, might readily be interpreted as acute rheumatic fever with the not unusual complications of pneumonia and tonsillitis. The prolonged and migratory character of the pneumonia, failure of involvement of the heart in so severe a process, the unusually high leukocytosis and polynucleosis, however, constitute marked deviations from the usual sequence of events in acute rheumatic fever, and it seems much more logical to attribute all of the phenomena to an acute pyogenic infection, which in this instance it would seem fair to assume was the Micrococcus catarrhalis, repeatedly recovered in pure culture.

Case II.—Lobar pneumonia with extensive pleuritis, complicated by diphtheria and erysipelas. Acute exudative nephritis as a sequel. Bacillus coli communis in pure culture from sputum. Recovery.

A Polish farmer who had been in this country three and one-half months was admitted to Bellevue Hospital on January 24, 1910. He was aged thirty-four years, and unmarried. About January 10, 1910, he began to have severe pain in his epigastrium after eating. This came on immediately after his meals, was constant, severe, and localized, but was relieved by vomiting, which occurred about one hour after eating. The vomitus consisted of food and often showed streaks of blood and his stools

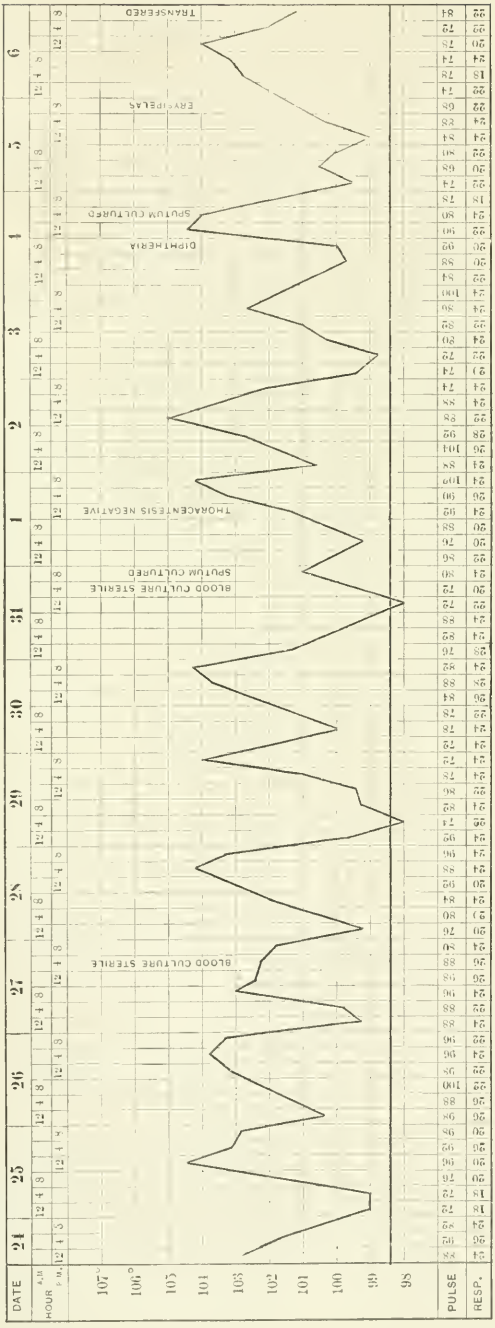

CHART II.—Lobar pneumonia with extensive pleuritis. Bacillus coli communis in sputum

also had often been blood streaked. He had lost no weight. During the week preceding entrance to the hospital, however, he had not vomited, but had become weak and frequently had chilly sensations.

Ten years previous he had had a similar attack of stomach trouble, which lasted one month and during which he once vomited a quantity of blood. He had since been well until onset of present illness. He was accustomed to drinking three or four glasses of beer and one or two drinks of whisky daily.

Upon admission the patient's temperature was 102.8°; pulse, 88; and respirations, 24. (See Chart II for course of disease and other data.) He was well nourished, his tongue was clean, and his mental condition was normal. His arteries were unduly thick and his pulse was dicrotic. His heart and lungs appeared to be normal, as did also his abdomen except for a moderate degree of bilateral tenderness and muscular spasm in his epigastrium. Liver, spleen, and kidneys were not palpable and his urine was normal. On January 21 his blood contained 21,000 leukocytes, with 83 per cent. of polymorphonuclears. A test meal of bread and tea removed in one hour amounted to 100 c.c.; total acidity was 66, free hydrochloric acid none, combined 50; lactic acid was present, but there were no blood cells. His stools contained no blood, visible or occult.

On January 26 patient began to cough and raise a little thin sputum, which was negative for tubercle bacilli. There were no abnormal pulmonary signs to be found. He did not vomit, and complained of no pain. No malarial parasites were found in his blood. On January 28, signs of consolidation appeared over the upper lobe of his right lung; also just within the angle of the right scapula was a small area of diminished resonance, increased fremitus, and bronchial breathing, which was surrounded by an area of vesicular breathing, diminished in intensity. The physical signs in his thorax remained the same except that the area of dulness over the right lower lobe increased in extent and the breath sounds so diminished in intensity that a pleural effusion suggested itself. A thoracentesis done on February 1, gave no fluid. Cultures of venous blood taken on January 27 and January 31 were sterile. Cultures made from specimens of "clean sputum" on January 31 and February 4 each showed Bacillus coli communis in pure culture.

On February 4 the patient developed a sore throat, from which Klebs-Loeffler bacilli were cultivated. On February 5 an erysipelatous infection appeared on his face. Because of the diphtheria he was transferred to the Willard Parker Hospital on February 6, and we are, unfortunately, unable to obtain any data regarding his condition while there. He was, however, returned to Bellevue Hospital on February 24. His temperature was then 98.8°; pulse,

80; respirations, 16; and he was in good general condition. Over the left lung posteriorly from the angle of the scapula down were dulness, diminished vesicular breathing, and many medium sized crackling rales close to the ear—signs of pleuritis with thickening of the membrane. Near the angle of the right scapula there remained a small area of consolidation just about as noted on January 28. The right upper lobe, previously involved, was normal. His abdomen was somewhat tender on deep pressure at the left costal margin.

The patient was without fever until March 1, when facial erysipelas recurred which lasted four days. On March 4, edema of his face and legs appeared and his urine indicated acute diffuse nephritis. He was very sick for three weeks, having several convulsions and marked anasarca. He gradually convalesced, however, and was discharged on April 16, in good general condition, his urine showing a trace of albumin only. There were signs of thickened pleura, but only few rales, the signs of consolidation of the right lung having disappeared.

The only unusual feature of this case was the recovery, on two occasions, of *Bacillus coli communis* in pure cultures from the sputum, which is rare in our experience. Clinically the most important feature of the pulmonary changes was the persistent consolidation in the right lower lobe, but which eventually resolved. We make no effort to correlate the gastro-intestinal symptoms with the pulmonary phenomena, and can find nothing in the literature which has any bearing on the case. The persistently slow pulse is suggestive and the leukocytosis, high for colon infections, is interesting.

Acute lobar pneumonia was for long thought to be caused by exposure to cold, and it was not until 1882–83 that this theory of its etiology was seriously disputed by Friedländer, who had found capsulated cocci, usually in pairs, in pneumonic lungs, and which produced in mice a septicemia with inflammation of the serous membranes, from the exudate of which similar cocci were recovered. This organism was later shown by Fraenkel to be what is now called Friedländer's pneumobacillus, though it is probable that some of the organisms with which he worked were really Fraenkel's pneumococci. In 1880 Sternberg and Pasteur had independently recognized what is now called the pneumococcus, but did not definitely connect it with lobar pneumonia. Koch and Eberth (1881), Leyden and Günther (1882), Matray and Ziehl (1883) recovered the same capsulated diplococci from the exudates of lobar pneumonia. However, in 1886, Weichselbaum reported the examination of exudates from 94 cases of undoubted lobar pneumonia and from all cultivated the pneumococcus. This appeared to definitely establish the etiology of the disease, though the chain of evidence was not completed until Gamaleia (1888), reproduced the characteristic lesions by

inoculating dogs and sheep with pneumococci. Further corroboration was much later had by the demonstration of a frequent accompanying pneumococcemia, Prochaska[1] having reported this in all of 50 cases cultured, and Rosenow[2] in 85 per cent. of 300 cases.

It has, however, long been recognized that Friedländer's pneumobacillus is the exciting cause of a small proportion of the lobar pneumonias; that in the pneumonia complicating typhoid fever *Bacillus typhosi* may be found; and in septic pneumonias the pyococci may alone be present. Schottmueller[3] has reported 5 cases clinically identical with lobar pneumonia, from all of which he recovered *Streptococcus mucosus*, and Hastings and Niles[4] have reported 43 cases of pneumonia, lobar in type, from the sputum of which pneumococci were not recovered by cultures. (The two cases here reported were included in their series.) That lobar pneumonia may be produced by a variety of microörganisms other than the pneumococcus cannot be doubted.

By a "clean specimen" of sputum we mean one which has been raised by deep coughing and expectorated into a sterile receptacle immediately after having thoroughly washed the mouth and gargled the throat with a saline or mild antiseptic solution. Kitasato's[5] method of handling sputum consists in picking out a more solid particle and washing it in several baths of sterile water, then opening it and smearing the fresh surfaces on proper culture media. If one carefully follows this technique a considerable proportion of pure cultures will be obtained.

The criticism that the bacterial findings in sputum may not represent the exciting cause of an inflammatory process in the respiratory tract is an obvious one, but the evidence for the correctness of the assumption is strong when the above-mentioned procedures are carried out. That the healthy respiratory tract is usually, if not always, sterile below the glottis is well established. Sputum may come from any part of the bronchial tree or from the alveoli, as, for example, the rusty sputum of pneumonia. Bacteria are usually found in the exudates from inflammatory processes excited by them. These are some of the reasons for attaching significance to the bacterial findings in sputum. Certain it is that in New York City many persons ill with a malady which cannot clinically or post mortem be differentiated from lobar pneumonia produce sputum which does not contain pneumococci. Neither can pneumococci be recovered from the blood of such patients.

We desire to acknowledge our gratitude to Dr. Thomas W. Hastings, who supervised the bacteriological work in connection with the cases here reported.

[1] Centralbl. f. innere Med., 1900, xxi, 1145. [2] Jour. Amer. Med. Assoc., 1907, xlix, 1799.
[3] Münch. med. Woch., 1905, lii, 1425. [4] Jour. Exper. Med., 1911, xiii, 638.
[5] Ztsch. f. Hyg. u. Infectionskrank., 1892, xi, 441.

SOME OBSERVATIONS ON THE SYMPTOMATOLOGY AND DIAGNOSIS OF CERVICAL RIB.

By Joseph L. Miller, M.D.,
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Symptoms due to cervical rib are apparently much more common than the reported cases would indicate. The papers of Keen,[1] Osler, Goodhart, and Francine, in this country, cover the majority of the reported cases. The German and French literature contains comparatively few reports. Its rather infrequent reported occurrence is the more interesting since the condition has been recognized anatomically since the time of Galen, although the first attempt to discuss the subject in detail was in the published paper of Hunauld in 1742. Gruber, in 1869, was able to find in the literature only 76 cases, and in 1894 Pilling collected 139 cases. Of this number, only 9 had been recognized clinically. As the rib is not usually palpable, it was not until the *x*-rays came into general use that a positive diagnosis could be made. During the past fifteen years the condition has been diagnosticated more frequently, still one is forced to believe that only a small percentage of the cases are recognized by the clinician.

During the last sixteen months 8 cases of cervical rib have been detected by the author. All of these had been previously diagnosticated as severe brachial neuritis. The *x*-rays and subsequent operation in five cases, with relief of symptoms, verified the role played by the extra rib. It is, perhaps, needles to say that a number of other suspicious cases failed to show a cervical rib.

In the recorded cases the *x*-rays show bilateral cervical rib in 80 per cent. of the cases, although in only 2 cases, as reported by Keene, were there bilateral symptoms. All but 1 of my cases showed bilateral ribs, and 2 complained of considerable distress in both arms. It is not infrequent to find the rib on one side more developed than on the other, and this was true in 2 of my cases. The pain in both instances was on the side of the larger rib.

Symptoms rarely appear before adolescence, and in many cases much later in life. In 1 of my cases the symptoms appeared at the age of ten years, in all of the others between the twentieth and thirtieth years. Unaccountably the trouble is much more frequent in females. All of the 8 cases presenting symptoms were women. Three patients complained of pain only in the left arm, 3 in the right, and 2 in both arms. In 6 of the 8 patients the onset was very

[1] For a complete review of the subject and bibliography, see W. W. Keen, The Symptomatology, Diagnosis, and Surgical Treatment of Cervical Rib, Amer. Jour. Med. Sci., 1907, cxxxiii, 173.

gradual and without apparent exciting cause. An attack of typhoid fever preceded the attack of pain in one instance, and another patient had her first intense pain after a fatiguing cold tramp in the woods. One patient was a violinist, but was compelled to discontinue playing as each effort precipitated an attack of pain that would persist for four or five weeks. The two factors most responsible for exciting or increasing the intensity of the pain were cold and the use of the arm. In every instance the pain was more marked during the winter months, and 2 patients were entirely free during warm weather. One patient for several years in the beginning, only had discomfort when the hand was placed in cold water. This would excite intense cramps in the hand with extreme blanching of the skin. The patient was so susceptible to cold that getting out of bed in a cold room would immediately excite an attack of pain. Two of these patients came to the office with the hand and wrist carefully wrapped in flannel or cotton to protect the extremity from the cold, although the season was only early autumn.

In every instance there was a tendency for the pain to become gradually more severe; the symptoms, at first infrequent and excited by cold or the use of the arm, gradually became persistent and developed without special exciting cause. The pain was usually described as dull in character, and in 4 of the cases was chiefly confined to the forearm and especially along the course of the ulnar nerve. In the other 4 cases the entire arm, shoulder, and interscapular region on the affected side were involved. One patient described the pain as "band-like" about the elbow and wrist. Three patients were able to obtain relief during the night by placing the hand on top of the head, but during cold weather this exposure after a short time would again excite the pain. One patient described the pain as "throbbing" in character, and noticed that it was synchronous with the pulse. On account of a marked thrill and bruit present in this case just below the middle of each clavicle an aneurysm had been previously diagnosticated. By changing position the patient would cause the bruit to disappear. At the operation it was found that a V-shaped notch had been worn in the rib by the subclavian artery, a branch of the brachial plexus lying between the artery and bone. There was a very slight dilatation of the subclavian above the notch.

Numbness and tingling are common symptoms even when patients are free from actual pain. Four patients complained of severe cramping in the fingers, usually either after exposure to cold or carrying even a light package in the hand. One patient had these cramps for ten years before acute pain appeared. She described the cramp as not especially painful, but found it necessary to use the other hand to straighten out the fingers. One patient complained of these cramps for almost a year after the removal of the rib, although free from all other discomfort. Paresthesia described

as a cold blast or cold water running over the hand, was complained of by 1 patient. In every instance the arm tired easily. Carrying a package, placing an object on a shelf, and even writing would cause a pronounced sense of tiredness and weight in the arm, which would disappear after a few minutes' rest. One patient noted long before the onset of pain that the right arm tired much more readily than the left. Using the arm usually excites attacks of pain. One patient who worked in a factory and was obliged to move light boxes from a shelf, after working a few days would suffer such intense pain that she was compelled to lay off. The pain would disappear after a few days' rest.

Vascular phenomena were noted in 5 cases. In 3 marked ischemia with cramping of the fingers would develop after moderate exposure to cold. The affected hand of 1 patient was continually pale, and would not redden when placed in hot water. Four patients (this included 2 who at times had ischemia) had cyanosis of the hand. In 1 patient with bilateral cervical ribs the pain was only present in the right arm; the cyanosis in the left. The cyanosis was especially marked when the arm was dependent, the contrast in color and temperature of the two hands being very striking. One of the patients, a trained nurse, had acquired a reputation for having one cold hand. This nurse for a period of several years was taking care of a patient with intermittent claudication. During the winter if the temperature became very low at night, he would complain of pain in his foot and she of her shoulder and arm. The patient had cyanosis of the foot and the nurse of the hand when that extremity was in the dependent position. Cyanosis occurred in 1 patient only after moderate use of the arm. This was the patient referred to above in whom the artery had worn a groove in the rib. In every patient with vascular phenomena a careful search was made at the time of operation to determine the cause. In only 1 case could we find any evidence of compression of the vein or artery. It is possible, traction of the rib on the tissues might have caused slight interference with the circulation, but if so it could not be demonstrated. It seems hardly possible that the vascular phenomena observed could be purely of nervous origin. In none of the cases was there any edema.

Atrophy was only observed in 2 cases. These were both long standing, one ten, the other fifteen years. The changes were confined chiefly to the interossei and thenar and hypothenar eminences.

It will be noted that the symptoms in this group of patients showed wide variation. The only constant complaint was a persistent intermittent or continuous disturbance in one arm. This is, perhaps, the most significant diagnostic point. Rarely does a simple neuritis continue for years. Another significant point is the marked susceptibility to moderate cold. Marked vascular disturbance, either ischemia or cyanosis, is unusual in simple

brachial neuritis. Significant is the acute exacerbation of severe pain after slight exposure or moderate use of the part. The relief obtained by position, especially placing the hand on the head when asleep, is very suggestive. Other points to be mentioned are weakness of the arm in the absence of pain, great intensity of the pain, a murmur over the subclavian, cramping of the fingers, especially after holding something in the hand, and finally, the progressive character of the trouble. Each year finds the patient more uncomfortable; either more pain or greater weakness, or both. In none of the cases could the rib be palpated. In quite a large percentage of the cases the symptoms were sufficiently characteristic to enable one to make a highly probable diagnosis without the *x*-rays; in other cases a cervical rib was merely considered a possibility. A good rule to follow is to suspect cervical rib in every patient with prolonged brachial neuritis, then confirm or refute the diagnosis by the *x*-rays.

Whether the cervical rib shows distinctly with the *x*-rays depends upon its size and more especially its position. It must be borne in mind that a very short rib may cause trouble, either by directly irritating the brachial plexus, or, more frequently, on account of the pressure exerted by a tendinous band extending from the tip of this short rib to the first dorsal rib. It is, therefore, important in patients with prolonged brachial neuritis, where the *x*-rays show only a very short cervical rib, to consider the possibility of pressure from this source. In one of the cases, a cervical rib had previously been suspected by another physician, but the *x*-rays were pronounced negative because it was thought to show only a long transverse process. On careful examination a short rib could be made out, which at operation proved to be about one-half an inch long, and connected with the first rib by a tendinous band. Since the operation the patient has been entirely relieved of the pain.

A cervical rib which curves abruptly anteriorly may be even more readily overlooked, and without careful examination by the *x*-rays may not be detected. Examination of the plate in such a case shows apparently only a rather prolonged transverse process, but just below the tip of the process a second shadow may be seen usually short and somewhat indistinct. This is the cervical rib curving forward and dipping somewhat downward, only this portion that projects below the transverse process shows in the picture. In 1 case the *x*-ray picture was reported negative in a patient with the clinical symptoms of cervical rib. Careful examination revealed a short faint shadow below the tip of the transverse process. A second picture taken at a different angle, gave a more pronounced shadow and at operation a cervical rib, more than an inch in length, was removed. This rib curved abruptly anteriorly, lying thus close to the spine, and for this reason was detected with difficulty by the surgeon. In cases of suspected cervical rib, it is, therefore, important to have pictures taken at different

angles, and then to observe the plate carefully for indistinct shadows.

The question would arise, whether in patients with severe prolonged brachial neuritis and negative *x*-rays, an exploratory operation should be made with the expectation of finding a very short cervical rib, the tendinous attachment causing the disturbance. Some of the English surgeons are operating on this indication with excellent results. When a patient has complained of severe brachial neuritis of unknown origin for more than a year, and treatment has failed to relieve, an exploratory operation might be warranted. It is advisable to warn the patient that after such an operation there may be weakness in the arm due to the manipulation of the brachial plexus, and that this may be of several months' duration.

Five of the 8 cases have been operated upon. Four were relieved of pain within a few weeks. One very severe case with cramps and marked atrophy had an occasional cramp on exposure to cold for more than a year after the operation, but was free from other pain. The atrophy is now much less and the patient is able to use the hand much better than for years. Another patient was relieved of the pain, but has complained of a great deal of weakness in the arm, not more marked, however, than before the operation. In this case eight months have elapsed, and as the weakness is gradually growing less, there is a good prospect for ultimate recovery. Only two months have elapsed since the last case was operated upon. This patient had complained of very severe pain for eight months. Since the operation the pain has been gradually subsiding until at present she is practically well. This is the only case where the pain did not disappear within two weeks after operation.

All of the patients have been pleased with the results of the operation. They have been entirely relieved of their pain, the arm in some cases is still weak, but judging from the course of the first case operated upon, almost two years ago, this weakness will probably entirely disappear.

SPONDYLITIS AND SOME OTHER FORMS OF VERTEBRAL DISEASE, WITH ESPECIAL REFERENCE TO DIAGNOSIS AND OPERATIVE TREATMENT.[1]

By B. Sachs, M.D.,

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At the completion of more than a quarter of a century of active neurological work, it is natural enough to review one's personal

[1] Read before the N. Y. Neurological Society, April 4, 1911.

experience and to stop to inquire what the chief surprises and disappointments have been in the diagnosis of nervous disease. Among the surprises I should be compelled to think, in the first instance, of the cases in which some form of vertebral disease had come to light when other troubles had been suspected. Among the great disappointments of neurological practice I should have to mention, first and foremost, the metastatic diseases of the central nervous system, and next to them the cases of some form of spondylitis in which, in spite of the fact that the lesion could be accurately localized, the physician and the surgeon appeared to be absolutely helpless. For the present I prefer not to touch upon the subject of the metastatic deposits of a malignant character in the brain and spinal cord,[2] and will confine myself altogether to the question of vertebral disease, to the difficulties of diagnosis, and to the question of operative interference in at least some of those cases. This entire question in its diagnostic and therapeutic bearings has been in my mind for more than twenty years, when it was suggested by the case of a young man whom I had occasion to see with Dr. Gibney and the late Dr. W. T. Bull. The patient was at the time in the incipient stages of an evident tuberculous spondylitis. When we saw him he was still able to get about, but was already showing the first signs of spasticity of the lower extremities. From this he went on to a complete spastic paraplegia, developed a marked kyphosis, upon which, in the course of time, incontinence of urine, bedsores, and marked sensory disturbances supervened. The patient was bedridden for at least a couple of years, and finally succumbed to his disease.

There were two things about this case which left a marked impress upon me. At this period—if the older men will recall it—in which the diagnosis of syringomyelia had been firmly established by the studies chiefly of Schultze and the other co-workers in Erb's clinic, many of the cases which up to that time had been diagnosticated as cases of progressive muscular wasting were recognized as cases of syringomyelia because of the peculiar dissociation of sensation. It was just at this time that the case to which I refer was of special interest to me, because in the earlier stages of this spondylitis this dissociation of sensation of the syringomyelic type was distinctly present until a more or less complete anesthesia up to the level of the lesion was established; and it was in this same case, that I recall distinctly, that I submitted the question to Dr. Gibney and Dr. Bull whether one could not make the attempt to get at the focus of the disease and thus possibly avert the paralysis which was developed subsequently, or possibly to check the tuberculous process. The surgeon and the orthopedist decided,

[2] This subject has been discussed at a meeting of the Neurological Section of the Academy of Medicine, April 11, 1911. See New York Medical Journal, July 1, 1911.

and perhaps wisely for the time, that surgical interference was not feasible. From that time on I have learned to regard dissociation of sensation as an early symptom of spondylitis, and I have kept the question of surgical interference actively in mind.

Let us take up the diagnostic question first, and let me refer briefly to a few histories of patients that have been observed during the last year or more in my service at the Mount Sinai Hospital, in which this factor of dissociation of sensation has been well established. These same histories will also subserve the further purpose of furnishing the text for the discussion of the more practical question of surgical interference. I prefer to limit myself to adult cases and not to touch upon vertebral disease as it is observed in children, although the reasoning that is applicable to the one series of cases might very well be applied to the other.

D. W., aged thirty years, a picture framer, was admitted to my service at Mount Sinai Hospital, October 20, 1910. He is married and has two children living and well. His wife has had no miscarriages. There is no history of venereal infection. He is not addicted to the use of alcohol or of tobacco.

Sixteen years ago he had typhoid fever. Fourteen years ago he was operated upon at Mount Sinai Hospital for osteomyelitis in the right thigh. Four years ago he fell while walking and struck his back. He had severe pain in the chest and back, causing inability to walk or to lie flat on his back for twelve weeks. Four months ago (May, 1910) he was caught in a heavy rain storm and was drenched thoroughly. That same night he suffered from severe pain in his chest. He had no chill or fever, but a painful cough without expectoration, which lasted for two weeks. The pain was severe at night while lying down. After two weeks the pain became constant in his left side about the level of the scapula. It was "sticking" in character and prevented him from lying down at night. It persisted up to the time of his entrance into the hospital.

July 11, when he awoke, he noticed that his left leg felt as if it were asleep. He had gone to bed the previous night feeling well, except for the pain in the left side. In bathing he noticed that while the water felt very hot to his hands, he did not feel the heat in his legs or the lower part of his body. He had the feeling as if the lower part of his trunk and thighs were asleep. The left leg "dragged" and felt heavy and weak. Later, he noticed that the appreciation of heat had returned somewhat in the left leg, but not at all in the right. There was no spasm of the leg at that time, and no paresthesia. The third week after the onset he began to use a stick because of the fear that he might fall. He was unsteady in gait, and noticed that when he sat still for any length of time he had difficulty in straightening out his legs. The patient thinks that the weakness in the left leg progressed, but the right remained stationary. There has been no sensory or motor disturbance in the upper part of the body.

For the past five or six weeks he has noticed that he has had difficulty in starting the flow of urine, and that he could hold his urine longer than usual. There has been no incontinence. The bowels are constipated. He complains somewhat of reflex spasm of both legs.

The examination of the patient showed no abnormal condition in the internal organs. There were several adherent scars along the inner part of the right forearm, and also the scar of the old osteomyelitis operation at the lower end of the right thigh.

There were no symptoms referable to the cranial nerves.

The left lower extremity was markedly spastic and paretic. The right lower extremity was only slightly weakened in power. Both knee-jerks were exaggerated; a patellar clonus could be elicited; bilateral ankle clonus and Babinski reflex were present. The gait was spastic, the left leg especially being dragged. The left abdominal reflex was greater than the right. No loss of muscle sense and no loss of the sense of touch. There was marked diminution of pain sense in the right leg. The right cremasteric reflex was greater than the left.

There was a zone of diminution of pain and temperature sense from the third rib down to the sixth rib, on both sides of the median line, and this was followed by a second zone extending to the eighth rib, in which there was still more marked diminution of pain and temperature sense. From the eighth rib downward, on the right side, and marked by the median line of the abdomen, there was complete loss of pain and temperature sense downward and including the right leg. On the left half of the body, while the sense of pain and temperature was preserved, it was somewhat diminished in acuteness below the eighth rib. Posteriorly the zone of diminished pain and temperature sense lay between the sixth and twelfth dorsal vertebræ. The area of complete loss of pain and temperature sense commenced at the twelfth vertebra extended downward, and included the right limb. The scrotum was sensitive to pain and to heat and cold. There was no tenderness of the spinal vertebræ, but there was rigidity of the lower cervical and upper dorsal vertebræ, and a certain amount of lordosis in this region.

The *x*-rays showed a spondylitis involving the first, second, and third dorsal vertebræ.

The diagnosis at this time was made of a probable tuberculous spondylitis with exudate compressing the cord and causing the Brown-Séquard symptom complex. The temperature varied from 99.6° to occasional rises of 101° to 102°, until November 21, when it began to rise gradually from normal to 102° and 103° evening temperature.

The blood cultures taken at this time were negative; 27,400 leukocytes, 79 per cent. polynuclears.

About this time the right thigh above the knee became swollen and very painful. A diagnosis of an osteomyelitic abscess was made.

The patient was transferred to the surgical service of Dr. Gerster. The abscess was incised and an osteomyelitic process of the lower end of the femur was discovered and removed.

Before he was operated upon it was felt that the abscess was of the nature of a psoas abscess and an apparatus for fixing the spine was devised by Dr. Nathan. The patient gradually began to recover power in the legs and the sensory disturbances began to disappear from above downward, so that when he was transferred to the surgical service, and before the operation on the thigh, he had regained full power in his legs, and the sensory changes had disappeared. Exaggerated knee-jerks and ankle clonus still remained in the left leg.

On March 19 he was discharged from the surgical service cured. The nature of the spondylitis remains uncertain.

Summing up the symptoms in this case, in which the diagnosis was uncertain for many weeks, we may say that the patient had an old osteomyelitic process in the right leg, the presence of which was confirmed by special *x*-ray pictures, and that the spastic condition of the lower extremity, the loss of vesical control, and the dissociation of sensation were due to the spondylitis. Some improvement was secured in this case by conservative orthopedic and surgical treatment. No attempt was made at active surgical interference of the spinal disease itself, and in view of the more or less diffuse character of the tuberculous disease of the vertebræ the possible beneficial effects of such interference remain distinctly problematical. But let us contrast with this case another which also presented a great many points of interest, and in which the diagnosis was puzzling up to the time of operation. The case deserves special attention because surgical interference was practised in a case of vertebral disease when we had some reason to suspect the presence of a spinal neoplasm. The result of the operation undertaken under these conditions has given us distinct hints as to what might be attempted in other similar cases.

S. T., aged fifty-eight years, a baker, was admitted to the surgical service of Dr. A. G. Gerster on November 5, 1910. In April he came to the Dispensary because of difficulty in breathing. Dr. Emil Mayer diagnosticated his condition as edema glottidis, and urged him to enter the hospital. The patient waited a few days until the condition became critical, when he applied for admission and was taken into the surgical ward. He was immediately operated upon for a retropharyngeal abscess, but no pus was found. During the operation he became asphyxiated and tracheotomy had to be performed. He was discharged from the hospital wearing the tracheotomy tube. He was readmitted to the surgical service in November for the purpose of closing the tracheotomy wound, and after admittance complained of a severe pain encircling his upper abdomen that began about four months previously and had gradually

increased in severity. He said he felt as if a cord constricted his abdomen in its upper part.

I examined him at this time and found that the fourth and fifth dorsal vertebræ were tender, and that the abdominal reflexes were lost. There were no other objective symptoms of involvement of the spinal cord. However, the character of the pain and its location, in addition to the tender vertebræ, led me to conclude that there must be something exerting pressure on the posterior spinal roots. An *x*-ray examination at this time was negative, and the condition of the throat was that of a peculiarly flaccid epiglottis which fell over the glottis in such a manner as to obstruct the passage of air. There was no evidence of neoplasm or inflammatory process anywhere. A few days later, examination revealed a hyperesthetic zone encircling the body at the level of the eleventh and twelfth dorsal vertebræ, and an area of analgesia extending in front from about one inch above the level of the umbilicus downward over both thighs, and in back from the level of the second lumbar vertebra downward over the buttocks, thighs, and legs. The legs and, in part, the soles of the feet were somewhat hypoalgesic. The knee-jerks were exaggerated. There was no ankle clonus, no Babinski, and no Oppenheim. There was no paresis of the legs. His gait was somewhat unsteady. No rectal or urinary symptoms. Lumbar puncture was performed and 10 c.c. of a clear, somewhat greenish tinged fluid was obtained. The fluid was under slightly increased pressure. It contained no cells and gave a negative Wassermann reaction.

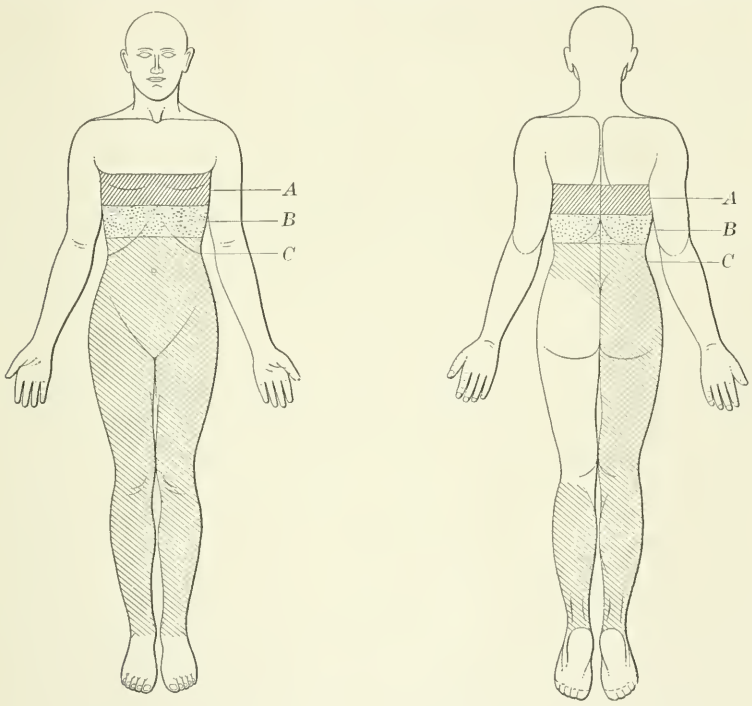
December 9. Patient now complains of formication in soles of both feet stating "they feel as if they weighed 300 pounds." There appears to be loss of muscular sense in the joints of the hallux. Bilateral Babinski has appeared and his gait is more ataxic. *X*-ray examination of the spine fails to show any abnormality. During the past week the patient has noticed that his urination has become delayed.

December 21. Patient's legs have become markedly paretic. He can move them, but can no longer stand. He complains very much of paresthesia in the feet and legs, especially of an intense burning sensation. The girdle pains are not so severe. Bilateral ankle clonus and Babinski persist. During the past six weeks the patient's temperature has reached 100° F. (rectal) on three occasions. The diagnosis was made of either an extramedullary neoplasm or some form of spondylitis, and exploratory laminectomy was advised.

The sensory status on December 21 was as depicted on the following charts.

The continuance of the symptoms, the very definite and strictly localizable disturbance of sensation, in which the pain sense was more affected than any other, made us urge operative interference in the hope of finding and possibly removing an extraspinal neoplasm or

some other morbid process. According to the areas of sensory disturbance, Dr. Gerster was advised to do a laminectomy, removing the fourth and fifth dorsal laminæ. Instead of finding a neoplasm, the surgeon at once came upon what appeared to be necrotic bone tissue, and removed as much of this as was practicable. It was early evident that only the lower part of the diseased portion of the bone was attacked and that the entire focus of necrotic bone tissue was not or could not be removed. In spite of this incomplete operation, the patient has distinctly improved, his pains are very much lessened, he



A, zone of hyperesthesia; B, zone of hyperalgesia; C, line marks beginning of analgesic area.

walks about with considerable ease, the sensory dissociation has disappeared (June, 1911). The question arises whether, in view of the satisfactory recovery from the first operation, a very much more radical procedure might not have been attempted, and, furthermore, whether even at this late day another operation might not be done to remove more of the diseased bone tissue. In this case, too, before and after operation, the study of the *x*-ray plates was of great assistance.[3]

[3] Case IV in Calwalder's recent paper appears to have been very similar. Frazier operated upon the patient. Coming out between the transverse processes of the fifth and sixth dorsal vertebræ was found a mass of . . . granulation tissue. Compression of the cord was relieved. (Amer. Jour. Med. Sci., April, 1911.)

Another case, not less puzzling in many respects than the preceding one, is that of R. J., a woman, aged sixty-four years, whose family history was negative as regards tuberculosis and carcinoma. Her past history was uneventful. She had never had any infectious disease or any cardiac, pulmonary, or renal disturbance. Her menopause had come on at about forty years of age. She was admitted to the Hospital September 8, 1910, and remained with us until January 14, 1911, when the needs of the service compelled her dismissal.

The facts that we could ascertain were that about nine months before admission to the hospital she began to suffer from "muscular rheumatism," which affected practically the entire body. About three months before admission she began to complain of a localized pain, a feeling of numbness in the small of the back. She stated distinctly that she had not had a fall. Soon thereafter similar pains affected the sole and then the toes of the right foot. About two months before admission the pain affected the entire right lower extremity, and one month previous to admission the left lower extremity had also become similarly affected. She had been confined to bed for two months on account of weakness of the extremities, the weakness increasing to such an extent that she was almost incapable of turning in bed.

The physical examination of the patient was negative with the exceptions now to be noted. There was slight nystagmus on extreme outward rotation. There were a few small anterior and posterior cervical glands. There were marked varicosities and ecchymotic areas on the anterior surfaces of both legs. Distinct weakness of the lower extremities with increased knee-jerks. There were no Oppenheim, Babinski, or Mendel reflexes; no ankle-clonus and no Achilles reflex obtainable. There was distinct weakness of the right peroneal group of muscles. Pelvic examination by Dr. Vineberg was also negative. The von Pirquet test was positive, a fact to which we did not, however, attach very much importance. On further examination we discovered that there was a marked kyphosis of the fifth dorsal to the tenth dorsal vertebræ. On very careful examination of sensation the entire body was found to be normal with the exception of the lower half of both lower extremities, in which there was a distinct diminution of temperature and pain sense, a little more marked on the right side. The other forms of sensation were well preserved.

During her long stay in the hospital the patient complained chiefly of pains in the lower portion of the back, of pains in the bladder which were due to a cystitis, and this in turn was probably responsible for the slight elevations of temperature which occurred; also of inability to sit up either in bed or in a chair without intense pain and discomfort. A Wassermann reaction which was taken proved to be negative. The *x*-ray examination showed a condition

which the radiographist termed a spondylitis deformans involving the first, second, and third lumbar vertebræ, and probably destruction of the fifth lumbar vertebra.

The kyphosis, the *x*-ray findings, and the general slowly progressive character of the symptoms encouraged us in the opinion that the case was one of spondylitis which was chiefly restricted to the lower dorsal and lumbar vertebræ, and responsible, no doubt, for the sensory disturbances as well as for the bladder symptoms with the loss of power. In view of the age of the patient it seemed impracticable to advise surgical interference, and the patient was removed to Bellevue Hospital, from there to Troy, where she lay until death occurred a few months later. The further development in the case we have not been able to ascertain. I have referred to this case as one in which, without the assistance given by the *x*-ray plate and the appearance of a dorsal kyphosis, the presence of vertebral disease might scarcely have been suspected. For the want of a better diagnosis conditions such as this patient presented might have been diagnosticated as senile paraplegia, and it is questionable whether some of these conditions are not occasionally due to chronic vertebral osteitis or possibly a chronic pachymeningitis with exudate.

I am reminded, in this connection, of a private patient, a young girl, aged twelve years, from Mobile, Alabama, whom I had occasion to see in 1906, and I refer to this case because, although the *x*-ray plate that was taken showed no tangible changes, there were two symptoms present which would have helped to localize the process. The question arises whether in such cases, if improvement is not obtained by fixation of the spine, surgical interference might not be attempted.

This child was the eldest of three children; normal birth; normal in every way; nursed up to ten months of age; measles at four years in very mild form. She had grippe in January, 1905. She did not recover speedily from this, and on examination of the sputum tubercle bacilli were found. She lived out of doors and seemed to be doing well. In January of 1906 she had an abscess in the ear, and ran temperatures resembling that of typhoid fever, as the home physician stated. She was thought to have an abscess of the kidney, and casts and albumin were found. No operation, however, was attempted. The radiograph that was taken proved negative. At that time she was seen by Dr. Achinard, whose observations were no doubt entirely correct. In March, 1906, she showed great weakness in the legs, which increased until the time of my examination in September, 1906. She was entirely helpless, and had been in a rolling chair for months. In the South a lumbar puncture was done in June, after which there seemed to be temporary improvement.

At the time of my examination she had a complete flaccid para-

plegia without any interference with the vesical or rectal reflexes. She was unable to stand unsupported. The right knee-jerk was diminished, the left was present.

The localizing symptoms in this case were the diminution of the knee-jerks, contrary to the usual occurrence in spondylitis, and the marked atrophy of the vasti group of the right leg, with diminution of the galvanic responses in the vasti muscles on that side, and, furthermore, distinct pain on pressure over the spinous processes from the eighth to the tenth dorsal, all pointing to a lesion that involved, in all probability, the lowest dorsal and possibly the first lumbar vertebræ. The child was put on the usual tonics, and I decided that no operation was to be attempted, although the question of operation had been submitted to me.

I ask the surgeons today whether, in such a case in which the symptoms, after all, proved that there was not, as yet, marked involvement of the spinal cord, operation should or should not be attempted? With the improvement in spinal surgical technique, a little more boldness in attacking these conditions would seem to be warranted.

I cannot regard the spinal column as a *noli me tangere*. It has been shown often enough, and again very recently by Cadwallader[4] that bone disease of very slight intensity may be associated with considerable exudate, and in some cases the body of the vertebræ may be affected very little indeed, while a small bone abscess may be giving rise to most of the trouble. It is well, perhaps, to bear in mind that in cases of intense bone disease with little compression, the paralysis, incontinence, and deformity of the spine may be early symptoms. But the cases which begin with dissociation of sensation, with marked girdle pains, or with radiating pains, with paresis rather than paralysis, with little or no vesical disturbance, are the cases in which the lesion is often extraspinal, possibly a chronic pachymeningitis, tuberculous or otherwise, with adhesions and exudate, and such cases are, to my mind, the proper subjects for operative interference at a very early stage of the disease. It is distinctly recognized that tuberculous pachymeningitis may occur without caries of the vertebræ.

In all these cases the two factors of compression and infection must be borne in mind. While the typical cases are, no doubt, cases of advanced bone disease and somewhat difficult to get at, both compression and infection may be due to extraspinal processes. I am not willing to believe that in such cases the fear of a general tuberculous infection should interfere with proper surgical measures.

The few histories that I have given must suffice as a basis for the two points which I have wished to elaborate in this brief paper. The one is the early appearance of dissociated sensation in

[4] Loc. cit.

vertebral disease, and the question of surgical interference. Dissimilar as these two points appear to be, they have some bearing, one upon the other, inasmuch as the early appearance of dissociated sensation should not only arouse the suspicion of vertebral disease, but inasmuch as this dissociated sensation is clearly a root symptom and points to the compression of these roots, either by the disorganized bony tissue or by an independent exudate, and inasmuch as these symptoms have often been observed long before the paralysis has become complete and before vesical or rectal symptoms have appeared, they are evidently prominent symptoms of a period at which surgical interference, if practicable at all, would be more beneficial than at a later period at which the presence of bladder and rectal symptoms, of complete paralysis, possibly of bedsores, or of marked kyphosis, show that the bony process has not only advanced to an alarming degree, but that it has impinged upon the spinal cord substance itself and has actually caused destruction of spinal cord tissue. When that stage has been reached operative interference will, of course, be of little avail.

In conclusion, let me urge that more attention be paid to the vertebral column, and that if, particularly with the assistance of the *x*-ray, a well circumscribed focus of bone tissue can be recognized, the surgeon shall attempt to get at the lesion. If the disease be in the body of the vertebræ the attack will not be an easy one, but this is a matter of technique which the surgeon must solve. The danger of general tuberculous infection, which was so great a factor in former days, should not play the important part it once did.

SPONTANEOUS INTRAPERITONEAL HEMORRHAGE.

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The large amount of work now being done on the chemistry and blood-pathology of the hemorrhagic diseases, has awakened lively interest in their clinical features as well. The patient here reported presented a form of spontaneous hemorrhage certainly very rare, possibly unique. All the usual causes of intra-abdominal hemorrhage were absent, and no definite origin for the bleeding could be found. There is some justification for regarding the case as a rare manifestation of the hemorrhagic disease; but the data are not sufficient for its positive inclusion in this clinical group.

The patient was a man, aged forty-eight years, who for twelve years had suffered from obstinate constipation, accompanied by

dull, heavy discomfort in the stomach. His previous history was otherwise negative. There was no history of bleeding in the family.

He was brought to the hospital in a serious condition, suffering from great abdominal pain. The onset of the illness had been with sudden acute abdominal pain about the umbilicus, four days previously. There was no nausea at the onset, nor had there been any since, though the patient vomited once, on the day of admission, after taking some tea. The bowels had not moved since the onset of his illness and there had been slight pain on urination. The abdominal pain was general; and had been constantly increasing since the onset. No history of injury could be obtained. The temperature was 101.5°, pulse 120, leukocytes 15,500. An enema was given in the ward on admission, and a large, constipated stool resulted.

The abdomen was generally and quite markedly distended, and moved but slightly with respiration; in the right iliac fossa it was held almost stationary. There was general abdominal tenderness. This was greater in the lower than in the upper half of the abdomen, most marked in the right iliac fossa, and very acute at McBurney's point. There was marked muscle spasm in the right iliac fossa; spasm was also present, but much less marked, on the left side. The outlines of the distended intestinal coils could be seen lying transversely across the abdomen, but no visible peristalsis was observed. No masses were anywhere felt. On percussion, the abdomen was everywhere tympanitic, except in the left flank, where the note was impaired. The impaired note reached forward to the level of the anterior superior spine and moved about two finger-breadths with shifts in the patient's position.

On rectal examination, resistance and tenderness were made out, and a mass felt which was thought to be in the wall of the rectum.

The signs were those of peritoneal inflammation, with fluid in the peritoneal cavity; and the case was regarded as one of peritonitis, in spite of the rather unusual history. The almost complete absence of nausea and vomiting were particularly striking, though I have observed three cases of appendiceal peritonitis during the past year, one of them a general peritonitis, in which all symptoms on the part of the gastro-intestinal tract were wanting. Intraperitoneal hemorrhage was not considered in this patient.

An exploratory laparotomy was done through a right rectus incision. On opening the peritoneal cavity, a large quantity of free blood escaped. The intestines were much distended, but the fresh blood was without odor, the serous coat of the bowel glistened almost in the normal way, and there was no sign of pus anywhere. A large amount, probably a liter, of blood was mopped out, and a systematic search made for the source of the hemorrhage. Liver, spleen, stomach, and kidneys were normal; and there was no evidence of abdominal aneurysm. There were numerous clots in the pelvis.

The patient was somewhat shocked by the operative manipulations and a rapid closure without drainage was done. He died about three hours later.

At autopsy, some fluid blood was found in the peritoneal cavity, but bleeding had evidently not continued since the operation. The operative manipulations had resulted in an early traumatic, general adhesive peritonitis, the intestinal serosa having lost its glister and the blood clots being loosely stuck to the bowel.

No source of the hemorrhage could be found. The solid organs were normal except for old, firm adhesions about the spleen. Near the cardiac orifice, the gastric mucosa was discolored by injection of the fine capillaries and by small, dark red ecchymotic spots. Similar areas were seen near the pylorus, and there were a few small ecchymoses in the large intestine.

On the serous surface of the bowel, about eight inches above the anus, there was an oval, dark purplish mass, measuring about 3 by 2 cm., evidently a hematoma in the bowel wall. Microscopically, sections of the intestine showed antemortem clots on the serous surface. The subserous vessels were widely dilated. In places there were hemorrhages between the muscular coats and the serosa.

Hemorrhages into the joints are common in "hemophilia;" and other serous cavities are mentioned in the text books, in a casual way, as rare sites for similar bleeding. But reports of such occurrences recognized during life, I have been unable to find; and the condition must be extremely rare. At autopsy, intrapleural and intraperitoneal hemorrhage are occasionally found in the so-called hemophilia neonatorum, and there is experimental evidence for the belief that spontaneous intraperitoneal hemorrhage does occur in the "hemorrhagic disease." In the Hunterian Laboratory of the Johns Hopkins Medical School, fatal spontaneous intraperitoneal hemorrhage has been observed by Whipple and Sperry[1] in dogs, in which the hemorrhagic disease had been artificially produced by chloroform poisoning. In these dogs, however, a hemorrhagic liver, which presented bloody blebs on its surface, was regarded as the source of the hemorrhage.

In a fairly complete search of the literature of recent years I have been unable to find a case identical with the one here reported. Mention, however, should be made of two somewhat similar cases.

Peck[2] reported a case of so-called hemorrhagic hepatitis with intra-abdominal bleeding. The patient, a man, aged twenty-three years, had awakened suddenly two days before admission with a sharp stabbing pain in the region of the gall-bladder. Headache and constipation were present, but no nausea, vomiting, or cough. The tem-

[1] Johns Hopkins Hospital Bulletin, September, 1909.
[2] Annals of Surgery, 1905, lxii, 597.

perature 103°, the pulse 112, the respirations 30, and the leukocytes 14,600. Rigidity and tenderness were present throughout the abdomen. The abdominal pain left as suddenly as it had appeared, but tenderness in the right hypochondrum persisted. The symptoms subsided, however, and the patient was kept under observation. Nine days after the onset a diagnosis of appendicitis was made and operation performed. A mild plastic general peritonitis was present, and the abdomen was found to be full of blood. The upper surface of the liver was adherent throughout to the diaphragm and its lower surface to the colon and mesocolon. It was uniformly enlarged. Its under surface was soft, spongy, and oozed with the slightest handling. This was regarded as the source of the abdominal hemorrhage and the case was reported, purely by way of description, as one of toxic hemorrhagic hepatitis.

Barber[3] has reported an intraperitoneal hemorrhage in a woman following labor.

Shortly after the normal birth of a normal child, symptoms of internal hemorrhage appeared, the onset following a "sudden sense of something snapping in the lower part of the back." Abdominal distention became marked, the pulse elevated, and a laparotomy was done. The peritoneal cavity was found full of fresh and clotted blood, for which no source could be made out. The case was, however, most probably a traumatic one and the hemorrhage due to some injury to the pelvic vessels during labor.

The case here reported, the case of Peck, and the observation on dogs suggest the possibility that intraperitoneal hemorrhage may be a feature of the hemorrhagic disease. In future cases careful blood studies should be made with reference to this point.

A CONSIDERATION OF SOME NON-TUBERCULOUS LUNG INFECTIONS.[1]

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With the advent of modern clinical and laboratory aids to the diagnosis of diseases of the chest, a reasonable popular demand has arisen for the earlier recognition of lung diseases. This demand is so insistent, the necessity of recognizing lung conditions while in a curable stage is so obvious, that the position of lung specialist has rightly assumed an important place in the field of medical achievement. Today, particularly in Europe, the tuberculosis

[3] British Medical Journal, July 24, 1909, p. 203.

[1] Lecture given before the Oakland College of Medicine and Surgery, February 27, 1911.

specialist occupies a justly imposing position, which increases in importance with the growing success attained in the early recognition and successful treatment of this malady.

Out of this progress, however, as was to be expected, a danger has arisen. Biological tests have been unscientifically applied and loosely interpreted in order to attain short cuts to diagnosis. Slipshod laboratory work has been accepted in place of painstaking investigation, with inevitably disastrous results to the diagnostician. The great prevalence of tuberculosis, together with the knowledge of the responsibility resting upon the practitioner, to the effect that he is expected to recognize this disease in its incipiency, has frequently caused him to overlook the relation which the physical signs and symptoms bear to conditions other than tuberculosis. Presumptive evidence of tuberculosis is too eagerly accepted, and the patient often sent to the sanatorium where the non-tuberculous nature of the malady is determined. Perchance, the error is not always discovered there and the subsequent history of the patient goes to make up a statistical record of cures, the result of the institutional treatment of tuberculosis, which is as startling as it is apparently satisfactory.

I do not desire to decry the efforts of the general practitioner to make early diagnoses, nor would I question the motives of those in control of sanatoria. The work achieved in the early recognition of pulmonary tuberculosis has saved thousands of human beings from untimely graves. On the other hand, indifference and incompetence, which have been responsible for the avoidable deaths of many whose disease should have been earlier recognized, have justly caused indignation. Far better that numbers of those non-tuberculous should be given the benefit of the doubt and be surrounded by the hygienic influences of life in well-conducted institutions, than that one who needs them should be deprived of these influences. All will agree, however, that the usefulness of such institutions will be seriously impaired unless more care in differential diagnosis is exercised by those who refer patients to and receive them into sanatoria.

Before proceeding to a consideration of some of the pulmonary infections other than those tuberculous, it will be well to briefly refer to certain physical signs due chiefly to anatomical peculiarities, and frequently found in normal individuals. My excuse for referring to these rather elementary facts is that these are the conditions mistaken for disease in a number of those referred to me as suspiciously tuberculous.

Relatively diminished resonance on percussion is usually elicited at the right apex. This has been variously ascribed to muscular development about the right shoulder, the position of the right lobe of the liver mechanically acting as a mute and thus modifying the percussion note and latent disease. None of these suggested

causes, however, satisfactorily explains the phenomenon. Auscultatory peculiarities of the right apex are present in many healthy individuals. The breathing takes on more of the bronchial type and vocal resonance is increased. Noted more than one-half a century ago by Skoda,[2] these phenomena have received general acceptation by all observers. The theory usually advanced in explanation is the difference in size and anatomical position of the right bronchus. Fetterolf's[3] recent study has, however, brought forth an explanation based on demonstrations on the cadaver. He has shown that almost entirely throughout its thoracic course the trachea lies in contact with the right lung, separated only by the parietal pleura and a delicate layer of areolar and lymphatic tissue; while on the left side the large bloodvessels, esophagus, and areolar and lymphatic tissue are interposed between the lung and trachea. With these anatomical facts in mind, Fetterolf assumes the phenomena present at the right apex to be due to the more direct transmission of vocal vibrations from the trachea through the tissues of the superior mediastinum to the right lung, rather than through the bronchial and pulmonary air. Another condition frequently mistaken for an adventitious chest sign is the shoulder-joint friction first mentioned by Gowers,[4] in 1876, to which more recently attention has been called by Gee.[5] This has subsequently been observed by Lord[6] and still more recently by Cooper.[7] It is usually heard over the scapular region, increasing to its point of maximum intensity over the shoulder-joint. It is frequently mistaken for a pleural friction, and especially when heard distinctly in the supraspinous fossa, has been considered evidence of apical disease.

Such physical signs when accompanied by symptoms suggestive of lung disease are frequently given false significance, as the following clinical record will illustrate:

The patient was a healthy looking man, aged twenty-five years, with a good family history and of temperate habits. Seven years previous to examination he had had typhoid fever, since which time he had been subject to colds, and had a troublesome morning cough, always bringing up some sputum. He was 10 pounds below his average weight, and was apprehensive of lung trouble. Intracutaneous and cutaneous tuberculin tests remained negative at the end of three days.

Examination: The chest was flat in type, symmetrical, with depressed clavicular fossæ on both sides. Tactile fremitus was increased over the upper part of the right chest anteriorly. There was dulness at the right apex to the second rib. Interrupted inspir-

[2] Abhandlung über Perkussion und Auskultation.
[3] Archiv. Int. Med., February, 1909.
[4] British Med. Jour., November 18, 1876.
[5] Auscultation and Percussion, p. 118.
[6] Boston Med. and Surg. Jour., October 21, 1909.
[7] Jour. Amer. Med. Assoc., vol. liv, p. 1865.

ation existed between the clavicle and the third rib on the left side. A friction was present over the left scapula increasing in intensity as the shoulder was approached. The breath sounds were diminished throughout both lungs posteriorly. The radiogram was negative. A marked induration of the nasal septum with a general nasal catarrh, together with considerable pharyngeal and laryngeal catarrh, revealed the cause of the persistent cough. The sputum microscopically showed nothing more than a large amount of epithelial debris.

Diseased conditions of the upper respiratory tract are frequent causes of cough. Given such a cough, unless the physical signs in the chest are carefully interpreted, and the upper respiratory passages thoroughly examined, frequent erroneous diagnoses of apical tuberculosis will be made, and while the unfortunate patient is restricted in his activity because of his supposed lung lesion, the condition predisposing to lung disease is allowed to progress unnoticed. I would like to offer here as an axiom that it is difficult to maintain healthy lower respiratory passages with the upper ones in a state of chronic disease.

To the clinician who requires more for the establishment of a diagnosis of pulmonary tuberculosis than a mere correlation of the physical signs and symptoms usually found where that disease is present; who has learned to thoughtfully interpret tuberculin reactions in the light of the susceptibility of the patient to different concentrations of tuberculin, so painstakingly demonstrated by Ellermann and Erlandsen,[8] Lossen,[9] and others; who realizes that the microscopic examination of sputum reveals more than the mere presence or absence of tubercle bacilli; to such an observer the conviction has come that the influenza bacillus, the pneumococcus, the micrococcus catarrhalis, and the pyogenic cocci form important etiological factors in a considerable number of chronic lung infections. Admitting this fact our conception of the great incidence of tuberculosis must undergo considerable modification.

Lord[10] has called attention to the fact that as only about one-half of the cases reported as cured in the statistics of institutions for the treatment of tuberculosis are proved by sputum analysis, it is probable that many non-tuberculous cases are included and the percentage of reported cures thus materially raised. Difficulties beset the diagnostician in the recognition of the true etiological factor in such cases. Chronicity is marked, many of these patients having coughed for years, even for decades. The physical signs usually present nothing different from what could be expected in a tuberculous lesion. It is often impossible to establish the time of onset of the acute infection and the disease seems to have begun insidi-

[8] Deutsche med. Wochenschr, 1909, No. 10.
[9] Beiträg zur Klink der Tuberculose, Band xvii, Heft 2.
[10] Boston Med. and Surg. Jour., May 11, 1905.

ously. Oftentimes the disease progresses to destruction of lung tissue and abscess formation, as is seen in advancing tuberculous lesions. Frequently extensive multiple bronchiectatic cavities exist, and the sputum may reach a large quantity, the clinical picture being identical with multiple cavity formation in phthisis. Pneumothorax and empyema are occasional complications. The *x*-ray examination oftentimes reveals the mottled shadowing such as is made by tubercles or the dense shading of extensive tuberculous disease.

It is in such conditions that important diagnostic information can be obtained from careful interpretation of tuberculin tests, based on the reactive capacity of the individual with an active tuberculous lesion to minimum quantities of tuberculin. Recent work with the intracutaneous tuberculin test[11] has convinced the writer that we have in this test a valuable method of applying tuberculin in such minute quantities as to differentiate active from latent tuberculous lesions in a large percentage of suspected cases. By this method as small an amount as $\frac{1}{1000}$ mg. is injected into the cuticle, care being taken not to penetrate the entire thickness of this membrane. No general reaction follows this procedure as follows the older and less delicate subcutaneous injection. It has the advantage over the cutaneous tests in that it admits of exactness of dosage, a condition *sine qua non* to the scientific application of diagnostic tuberculin tests.

Repeated examinations of the sputum probably form our best means of differential diagnosis, particularly in chronic influenzal infections. The almost constant presence of the influenza bacillus in well-washed specimens, together with a preponderance of the polynuclear cell element in the sputum afford evidence of great diagnostic value. Wolf-Eissner[12] has called attention to the significance of the presence of large numbers of lymphocytes in tuberculous sputum, and I wish here to emphasize this very valuable diagnostic fact. The frequency with which tubercle bacilli were subsequently found in sputum in which lymphocytes were present in large numbers, has taught me to recognize in the presence of the latter, valuable evidence of tuberculous disease.

It is fitting at this time to protest against the slipshod methods too frequently applied in the search for tubercle bacilli in the sputum. By the usual smear method of examination, bacilli, unless in large numbers, are frequently overlooked. At the present time, my laboratory assistant is engaged in the preparation of a report to be published shortly in which a series of sputum specimens are being submitted to four different methods of examination; namely, (1) the ordinary smear method; (2) incubation of the sputum and

[11] Evans and Whitney, Archiv. Int. Med., September, 1910, vi, 307.
[12] Frühdiagnose und Tuberculose-Immunität, 1909.

examination of smears made from the centrifuged sediment; (3) the antiformin method, and (4) the method of Ellermann and Erlandsen. The result of this work has proved most interesting and demonstrates the fallacy of relying on the findings of the ordinary laboratory technique in sputum of a small bacillary content. Conversely, too little attention is paid by laboratory workers to the morphology of the tubercle bacillus, and as a result other acid-fast bacilli and artefacts are frequently mistaken for the bacillus of tuberculosis. The danger of this mistake is great owing to the prevalence of such bacilli. They are frequently found in the contents of tonsillar crypts, in nasal secretions, in food products, such as butter and milk, and sometimes in the sputum of patients with bronchiectasis and putrid bronchitis. They do not resist alcohol as do tubercle bacilli and, therefore, the latter should always be used as a decolorizing agent. The majority of them grow readily on the ordinary media, so that confusion should usually not arise. In cases of doubt, guinea-pig inoculation should be undertaken.

The influx of tropical diseases into California following our Oriental conquests has given rise to much interesting material for study. Sometime ago I heard David Starr Jordan emphasize the necessity of a large endowment for the founding an institution in California for research work in tropical diseases. Among the many interesting conditions incident to the introduction of tropical diseases is that caused by the trematode, Paragonimus westermanii, or Distoma westermanii, producing the so-called lung-fluke disease. This parasite, well described by Stiles,[13] probably enters man in embryo form with contaminated food or water, passing either direct from the mouth to the bronchi, or through the stomach and thus by the lymphatics to the lung.

The pathology consists of multiple small cyst formations sometimes situated deeply in the lung tissue, but usually superficially or immediately under the pleura. These cysts contain the parasites in varying numbers. Sometimes the septa between cysts may break down, forming a considerable cavity. The lumen of these cysts or cavities communicates directly with the adjacent bronchi and thus the ova, together with the caseous material and fluid contained in the cysts, are expelled in the sputum.

The symptoms strongly suggest a tuberculous infection. The onset is usually gradual. There are recurrent attacks of hemoptysis. Hoarseness and a chronic cough develop. The sputum is of a yellowish-red, dusty-brown color and contains the ova of the parasite in varying numbers, which should always be examined in fresh unstained specimens. In addition to the eggs, Charcot's crystals, blood, pus, and alveolar and bronchial cells are found. The recur-

[13] Bulletin 17, Hygienic Laboratory, U. S. Public Health and Marine Hospital Service; Osler's Modern Medicine, i, 536.

rent hemoptysis frequently gives rise to a severe grade of anemia. The temperature is but slightly, if at all, elevated. Physical signs sometimes simulate those found in tuberculous disease. Retraction of the thorax, with unilateral or bilateral signs appreciable on percussion are frequently observed. The breath sounds may be diminished, sometimes they are bronchial in quality, and there may be dry or moist rales. The discovery of the ova in the sputum establishes the diagnosis.

The prevalence of the disease among the Oriental population of California is probably greater than is thought. Fehleisen and Cooper[14] have reported a case found in San Francisco. It is not at all impossible that the reported high mortality rate from tuberculosis in our Oriental population can be explained by the fact that pulmonary distomatosis is frequently unrecognized.

No recent discovery has brought to the medical mind such an appreciation of the marked prevalence of syphilis as has the practical application of the complement fixation test of Wassermann. Recognizing this great prevalence, it is nothing short of startling, that apparently we seldom see manifestations of syphilitic infection in the respiratory organs. The explanation of this phenomenon, I believe, is owing to the fact that this condition is frequently unrecognized. Admitting this fact, is it not possible that the satisfactory results reported within the last few years from the mercurial treatment of pulmonary tuberculosis may appear in a new light?

While secondary manifestations of syphilis may present lesions in the trachea and bronchi, and be accompanied by other secondary symptoms which make diagnosis comparatively easy, the tertiary lesions present difficulties in the way of correct diagnosis which make recognition oftentimes impossible unless the rather laconic admonition of Dieulafoy is faithfully observed, namely, that the true means of arriving at this diagnosis is to think of syphilis. The above named investigator has divided lung syphilis into six distinct types,[15] which division presents such an excellent classification that I quote it verbatim: (1) Pulmonary syphiloma, with acute febrile course, simulating acute tuberculosis or tuberculous bronchopneumonia; (2) pulmonary syphiloma of slow course, simulating ordinary chronic tuberculosis and phthisis in the stage of cavity; (3) broncho-pulmonary syphiloma, with fibrosis or sclero-gummatous lesions, simulating chronic pneumonia and cirrhosis of the lung, with or without bronchial dilatation, pleurisy, and tracheobronchial adenopathy; (4) syphilitic gangrene of the lung; (5) syphilitic pneumopathy, complicated by pulmonary tuberculosis; (6) hereditary pulmonary syphilis.

With this rather elaborate but practical classification, it will at

[14] Jour. Amer. Med. Assoc., vol. liv, p. 697.

[15] Clinique Médicale de l'Hotel-Dieu, 1898, lecons 18 et 19.

once be seen that syphilis may present a clinical picture that can fit almost any tuberculous lung condition. A consideration of the pathology of this interesting condition is beyond the confines of this paper. For this, I would refer you to the excellent articles of Fowler and Godlee[16] and Dieulafoy,[17] an English translation of the latter having recently appeared. Certain pathological features will however, be briefly mentioned in order to arrive at a better interpretation of some symptoms and physical signs which may prove of value in differential diagnosis. While the apex of the lung is the usual site of beginning tuberculous infection, the root and central part of the lung is a favorite location of a syphilitic lesions. If unaccompanied by tracheal or bronchial lesions, such a condition may give rise to no signs or symptoms pointing to the diseased process. With the advent of stenosis of the main bronchus, progressive destruction of lung tissue may ensue as in a tuberculous lesion. In nearly all cases of such destruction in syphilis, stenosis of some main part of the bronchial tree is present. This gives rise to what, I believe, to be the most prominent symptom of luetic lung lesion, namely, dyspnea, a dyspnea often entirely out of proportion to the apparent pulmonary condition, sometimes becoming paroxysmal and assuming the character of bronchial asthma.

While both tubercles and gummas may undergo necrosis and caseation, softening and cavity formation is the rule in tubercle, the exception in gumma. Expectoration, therefore, will be scant, unless destruction has progressed as a result of bronchial stenosis, when, of course, the profuse, purulent, fetid sputum of bronchiectasis may be met with. With extensive destructive lesions the general symptoms do not differ materially from those of advanced tuberculous disease.

Tuberculin tests probably do not offer as great aid in differential diagnosis here as in other non-tuberculous lung affections. Constantini[18] found the intracutaneous tuberculin test positive in all but 3 out of 47 syphilitics so tested. Wassermann reactions were also positive in all these cases. He does not believe that local tuberculin reactions can be utilized for the differentiation of syphilis and tuberculosis.

Repeated examinations of the sputum together with careful sifting of the history and thorough search for evidence of syphilis elsewhere on the body, rather than the result of the physical examination of the chest, must remain our most useful means of recognition. Dieulafoy probably did not go beyond the confines of conservatism when he said, "In a suspected case of pulmonary tuberculosis let us always think of the possibility of syphilis; in dealing with a patient considered as a case of incurable phthisis, let us still

[16] Diseases of the Lungs, London, 1898.

[17] Manuel de Pathologie Interne.

[18] Policlinico, Rome, November 27, 1910, xlviii, 1507.

think of syphilis, and if repeated examinations of the sputum show the absence of Koch's bacillus, let us have immediate recourse to specific treatment."[19]

I would add to the last postulate, the necessity of first applying the complement fixation test in all such questionable cases. While the frequency of positive Wassermann reactions has caused us to modify our preconceived ideas regarding the permanent cure of syphilis, it has placed the prevalence of this disease in an entirely new light. The diagnostic knowledge attained by its application has unfolded to us opportunities for therapeutic endeavor undreamed of before, which has reacted beneficially on great numbers of sufferers, whose condition would have remained hopeless, had it not been for this discovery.

An interesting chapter might well be added in a consideration of lung infections due to mycetes. Though the first cases recorded of the presence of fungi in the lungs were by Virchow, as long ago as 1854, and though much has been written descriptive of the lesions produced by actinomyces bovis, the classification of mycotic lesions has been much neglected and today considerable confusion exists regarding the role played by the oidium, the blastomycetes, the aspergillus, and probably a number of other fungi concerned in the various forms of pulmonary mycosis. Much discussion has arisen regarding the pathogenicity of some of these fungi. In some instances they are undoubtedly found incidental to infections with well-known pathogenic bacteria. It is quite possible that their presence in some cases may have been due to postmortem change. Actinomycosis, however, has been generally recognized as a disease in the human being. When we realize that one English observer has seen in his practice five cases in a little more than a year, it must be acknowledged that it is more common than is generally supposed. Its lesions produce a symptom-complex easily confused with that caused by tuberculous disease. Weakness, gradual loss of strength, anemia, and cough, with or without expectoration, accompany the gradual onset of the disease. Loss in weight and appetite with some fever follow. Localized dulness with weakened breathing over the dull areas may suggest tuberculous consolidation or empyema. Later, signs of cavity formation occur. The sputum, if carefully examined at this time, will probably contain the yellow granules characteristic of the ray fungus. Unfortunately in the search for tubercle bacilli, these other bodies are too frequently overlooked. Even in a later stage, when the chest wall becomes involved followed by softening and destruction of these structures, the condition is likely to be mistaken for empyema or a carious rib, when careful examination of the discharge would at once reveal the true nature of the lesion.

[19] Loc. cit.

Primary malignant disease of the lung is a rare condition, but metastases into the lung from a primary sarcomatous or carcinomatous lesion elsewhere, may frequently occur. Thus, cancer of the breast is frequently the cause of a subsequent metastasis in the lung. Less frequently, cancer of the lung is the result of the disease in the stomach, intestines, or other abdominal organ, spreading either by means of venous emboli through the portal vein, the vena cava, and thus through the right heart to the lung, or by means of the lymphatics.

In suspicious lung lesions, evidence of malignant growth elsewhere should carefully be sought and careful consideration made of the significance of previous operative procedures. Had the writer a few years ago, with a patient under his care with symptoms and physical signs strongly suggestive of tuberculous pulmonary disease, relied more on the significance of the evidence of previous removal of the breast because of cancer than on the history of tubercle bacilli having been found in the sputum, he would have been spared the chagrin of the true nature of the malady being revealed only when a bloody pleural effusion occurred shortly followed by death. Cancer of the lung when confined to that organ may give rise to no symptoms other than those usually found in bronchitis, and the true nature of the condition may be only discovered postmortem. Dyspnea is a prominent symptom and is usually more or less constant. This is especially the case when the lesion involves the mediastinum and produces pressure upon the lower portion of the trachea. As in syphilis of the lung, the dyspnea is out of proportion to the physical signs. Hemoptysis is present in a considerable number of the cases, sometimes the result of erosion of fair sized pulmonary branches, or due to the congestion and edema occurring in the pulmonary tissue surrounding the tumor nodules. The amount and quality of cough is dependent upon the location and size of the neoplasm. If the latter has undergone softening, there will be considerable expectoration which possesses the peculiar red currant jelly or prune juice character. In this material cancer elements and elastic fibers are frequently found. Hare mentions the presence in the sputum of unpigmented polymorphous cells of different sizes in which both nuclei and nucleoli show plainly. These cells are claimed to be pathognomonic of cancer. The pleura is frequently involved with resulting hemorrhagic pleural effusion, as in the case above mentioned. The physical signs frequently reveal nothing conclusive as to the true condition until the neoplasm attains a large size, or until it invades the mediastinum, when manifestation of pressure upon the structures there located will suggest the true nature of the lesion.

I have endeavored here to portray some of the pathological conditions most likely to be confused with tuberculous lung disease. I have omitted a consideration of some conditions rarely found,

which are more of academic than practical importance. Bronchial stenosis has been only briefly referred to in connection with what has been said on lung syphilis. A more detailed consideration of it would not be practicable here, without taking up the subjects of bronchiectasis, diseases of the bronchial glands, emphysema, mediastinal tumors, and other pathological conditions which stand in intimate relation to it, either in the role of cause or effect. This subject alone could well afford material for a future discourse.

Pulmonary fibrosis coming on as a sequel of pneumonia, or following bronchiectasis, or appearing as the result of the inhalation of irritating substances or dust, the so-called "knife-grinders' phthisis," or anthracosis has been omitted because of the fact that the repeated finding of tubercle bacilli in the sputum of these patients leaves little doubt that they are mainly of tuberculous origin. What has been presented will, I believe, illustrate some of the difficulties which beset the diagnostician in his effort to accurately differentiate some of these perplexing lung conditions.

In conclusion I desire to emphasize the importance of a more thorough correlation of clinical and laboratory investigation. After painstaking physical examination has been made and the results interpreted in the light derived from careful consideration of the history and symptomatology; after conservative estimation of tuberculin reactions and with a true appreciation of their limitations; after radiography has been utilized and its sources of error obviated by more careful preparation and interpretation of *x*-ray plates; even then in many of these perplexing condition, the rock on which the diagnostician must stand will be the exact knowledge attained by modern laboratory methods.

X-RAY STUDIES OF SEROFIBRINOUS PLEURITIS.[1]

By Wm. Engelbach, M.D.,
and
R. D. Carman, M.D.,
St. Louis, Mo.

Collections of fluid in the pleura, on account of their dense *x*-ray shadow, lend themselves especially to Röntgenological investigations. These *x*-ray studies have developed many new facts which are at variance with the accepted laws and theories governing the physical properties of pleural fluids; the most notable of these investigations relate to the inflammatory effusions, both of the costal and visceral pleuræ. The object of this paper is to

[1] Read before the Meeting of Röntgenologists of the Middle West, Chicago, April 8, 1911.

emphasize the many new points made clear by diagnostic methods which have elucidated the true anatomicopathological properties of these exudates in contradistinction to what has been hitherto wrongly accepted under the form of classical descriptions of these conditions. The salient points which will be given most consideration concern the interpretation of the physical conditions produced by these effusions,[2] an accurate understanding of which will be of aid to both the clinician and the Röntgenologist.

COSTAL OR PARIETAL PLEURISY.

The classic picture of this variety of pleurisy with effusion which dominates the text-books and literature is that of a mobile collection of fluid in the inferior portion of the upright chest, producing a dislocation of contiguous organs (Figs. 1 and 2). The well-

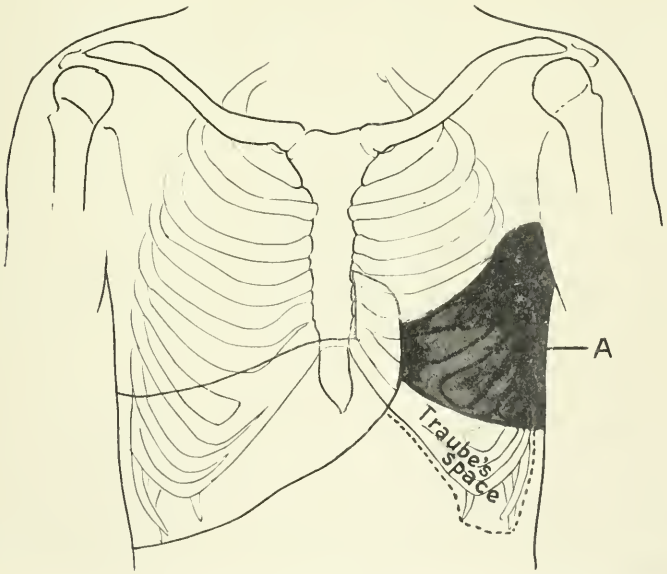

FIG. 1.—Diagrammatic illustration (anterior view), left-sided serofibrinous pleurisy with effusion in inferior portion of the chest. (Sahli's Diagnosis, p. 203.) Traube's space (between dotted lines) partially obliterated. No displacement of heart is shown.

known physical findings of mobile dulness in the lower part of the chest (patient in the upright position) not transmitting voice, breath, or whispered sounds, depending in extent upon the amount

[2] Only those cases which could be classified under simple serofibrinous pleurisy, *i. e.*, having a serous effusion by cytodiagnosis, have been used as the basis of this article. No attempt has been made to classify the cases with regard to etiology or duration.

of the effusion, having an Ellis' or Garland's S-shaped line along the lateral boundary of the chest, and Skoda's phenomenon bordering the dulness above, has been so firmly ingrafted upon the medical mind, as to be the anticipated finding in every case of pleurisy with effusion. Many texts still contain diagrammatic illustrations, demonstrating how the pleural effusion, having these characters in the upright position, gravitates to the median or lateral side of the pleural cavity, in response to changes in the position of the patient. These classic descriptions have been based upon the supposition that all pleurisies are in the lower portion of the upright chest, and that the fluid is more or less mobile.

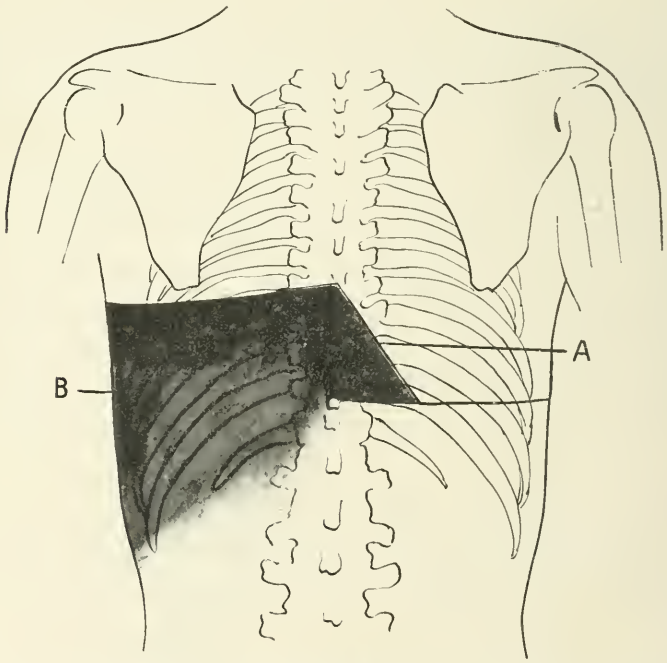

FIG. 2.—Same as Fig. 1, posterior view, showing *A*, Grocco's triangle, opposite the effusion (*B*).

That this is the exception rather than the rule, we have attempted to prove by giving illustrations of cases describing the common anatomical and pathological conditions existing in this disease. There have also been a number of other physical findings which have never been satisfactorily explained upon the basis that these effusions *always* occupy the lower portion of the upright chest. Among these are the following: (1) The presence of tympany over Traube's space with a left-sided pleurisy; (2) the presence of physical findings of fluid posteriorly and not anteriorly or vice

versa; (3) the contention regarding Ellis' or Garland's S-shaped line; (4) the absence of displacement of organs with apparently large effusions; (5) the absence of Grocco's sign in some cases of pleurisy with effusion; (6) the variation in the degree of dulness in apparently similar collections, etc. An attempt at explanation of

FIG. 3.—Skiagram of right-sided pleurisy with effusion, with patient in horizontal position: *A*, serous exudate. Note the upper line of the fluid is high toward the lateral side, but remains in the lower part of the chest in this (dorsal) position; *B* heart and vessel shadow.

these and other confusing findings induced the authors to make a combined clinical and skiagraphic investigation of 50 cases of simple serofibrinous pleurisy, upon which the conclusions of this article are based. In these cases the physical findings have been compared with fluoroscopic and skiagraphic examinations, and, with the exception of 8 cases, controlled by aspiration of the chest and cytodiag-

nosis of the effusion. These studies have led to many surprising developments bearing on the physical character of these effusions, particularly with regard to the location and mobility of their fluid, and the change of position of contiguous organs produced by the same. Space does not permit detailed accounts of individual cases; we have, therefore, confined ourselves to a summary of our findings in the common types of these pleurisies, which are at variance with the classic physical findings.

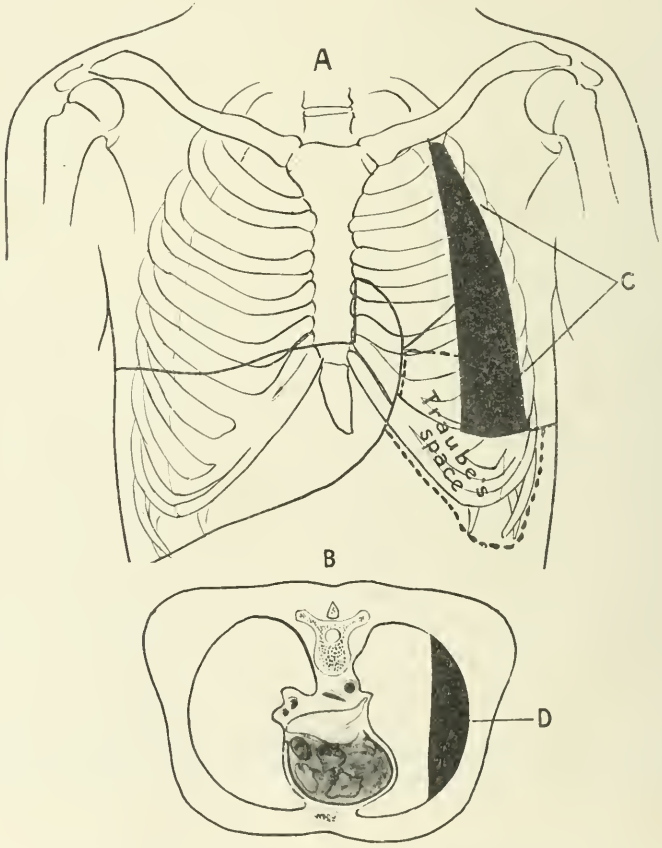

FIG. 4.—*A*, diagrammatic illustration of left-sided effusion in a vertical column in the upright chest. This location of the exudate will not completely obliterate Traube's space, displace organs, or produce Grocco's sign; *B*, cross-section of Fig. 4, *A*.

The Location of the Effusion. The greatest confusion has arisen from the misconception concerning the location of the effusion in the chest. The following demonstrations prove conclusively that these effusions are located in the majority of cases, not in the *lower* portion of the upright chest, but, on the contrary, occupy

variable positions in the chest. The fluid does not, as a rule, collect in the lower portion of the upright chest; this occurred in only 25 per cent. of our cases, as demonstrated both by physical and x-ray examination (Fig. 3). In the remaining 75 per cent. the location of the effusion occupied extremely variable positions in the pleura. In almost 25 per cent. of the cases, the fluid was in a vertical column in the lateral portion of the chest, compressing the whole lung toward the mediastinum (Figs. 4 *A,B*, and 5). In 34 per cent. of the cases the fluid was in a vertical position, enveloping the lateral aspect of the lung and extending nearer the median line posteriorly

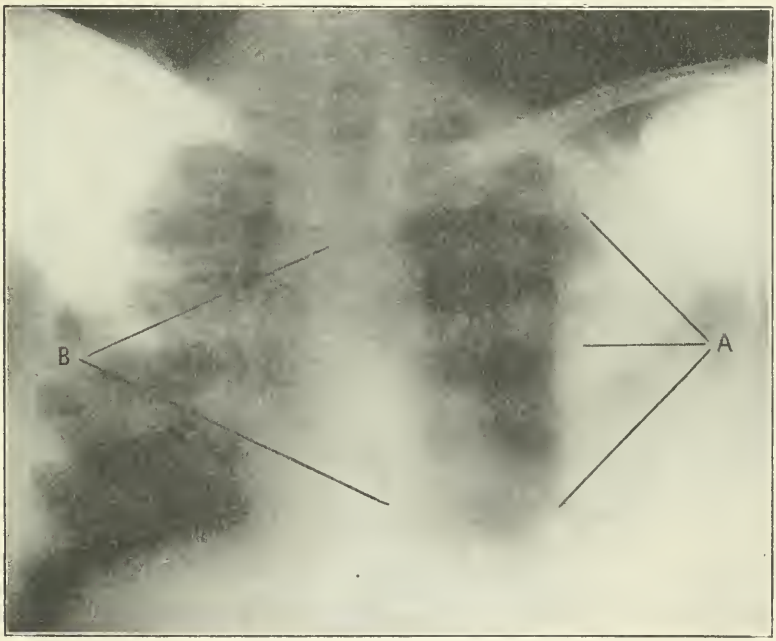

Fig. 5.—Positive skiagram—note shadows light instead of dark as in negative. Skiagram of left-sided effusion in a vertical column in the upright chest: *A*, effusion; note the uniform density of shadow and straight inner margin; *B*, heart mediastinal shadow slightly displaced to the right.

than anteriorly (Figs. 6 *A,B*, and 7). These effusions are best appreciated by studying stereoscopic skigraphs of the case. In about 16 per cent. of the cases a fluid occupied more or less of an upright position producing an oblique line across the chest, extending from above downward and inward (6 per cent.) or in the posterior portion of chest (9 per cent.) (Fig. 8), depending upon the size of the effusion. The smallest amount of exudate occupied the costophrenic angle of the pleura with the marked concavity of the shadow inward and upward. These Röntgenologic findings support the theory that the location of the fluid depends upon the position

assumed most constantly by the patient during the acute inflammatory stage of the disease. For instance, if the patient is constantly upon his back, during this stage, he may have a collection of fluid limited to the posterior portion of the pleural cavity; if he

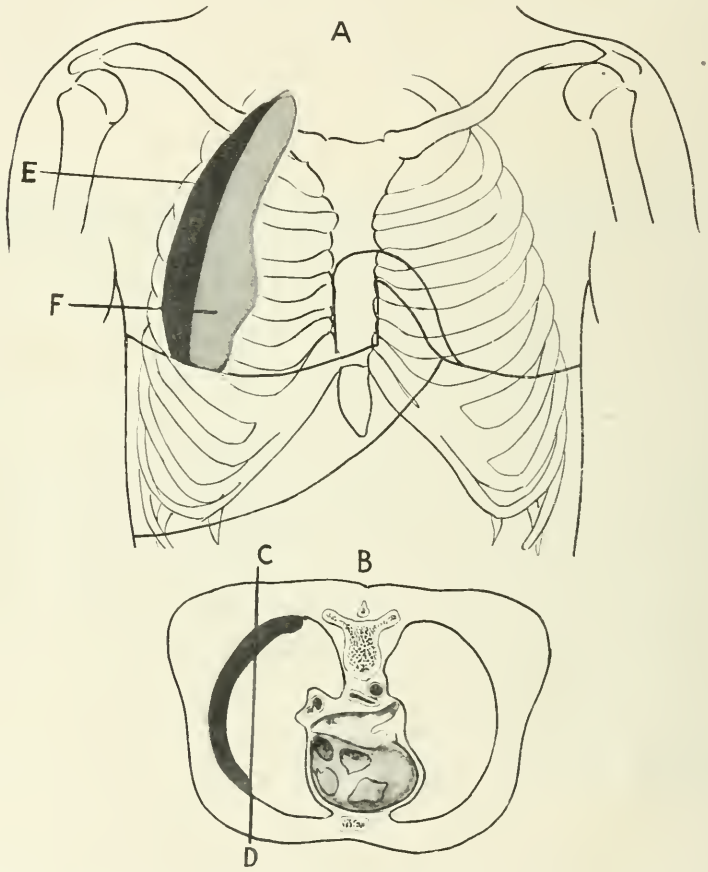

FIG. 6.—A, diagrammatic illustration of right-sided pleurisy with effusion, vertical column of fluid enveloping the lateral aspect of the lung, extending near the median line posteriorly than anteriorly; *B*, cross-section of the above; *C*, *D*, line projected through chest, showing how the *x*-rays external to this line passed through two thicknesses of fluid and those internal to the same passed through one thickness of fluid, explaining the differences in density of the shadows on each side of this line in Fig. 7.

is in the lateral position, the effusion may be confined to the lateral part of the chest; and if in the upright position, to the lower portion of the chest, etc.

Mobility of the Effusion. Contrary to the usual teaching, the effusion in pleurisy does not have the hydrostatic properties of fluid within a free non-encapsulated space. Fluoroscopic and skiagraphic examination of the above cases confirmed the work of

others who have demonstrated by physical findings that these pleural exudates are slightly, if at all, mobile. Many of the exudates occupying the lower half of the upright chest (Fig. 3) re-

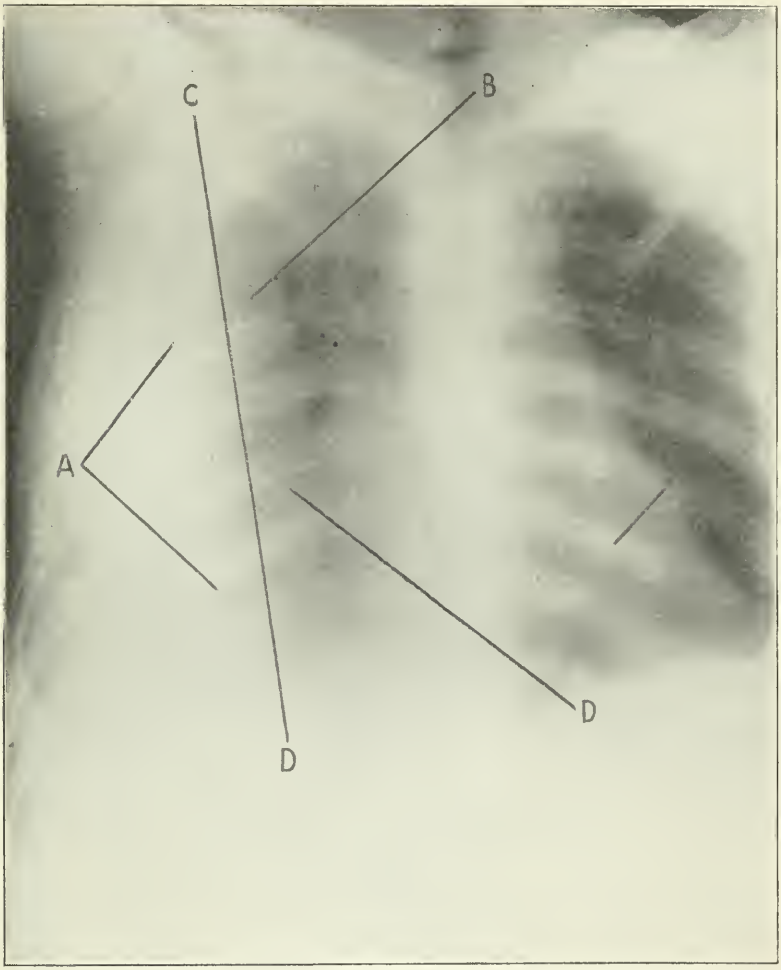

FIG. 7.—Positive skiagram—shadows light instead of dark as in negative. Skiagram of right-sided pleurisy with effusion. Vertical position of fluid enveloping the lateral aspect of the lung extending nearer the median line posteriorly than anteriorly: *A*, shadow produced by two thicknesses of fluid; *B*, posterior shadow produced one thickness of fluid posteriorly; *C*, *D*, line described in Fig. 6; *E*, heart shadow.

mained in this position when the patient was turned in the lateral or dorsal position for Röntgenological examination. In all of the cases in which the fluid occupied a vertical position in the pleura of the upright chest (Figs. 5 and 7) the shadow was absolutely

unchanged when the patient was placed in the lateral or dorsal position during *x*-ray examination. This was also true of those cases in which the fluid shadow occupied a more or less oblique position in the chest. These locations of more or less immobilized exudates can only be explained by the formation of adhesions encapsulating the fluid within certain definite limits. This is an important diag-

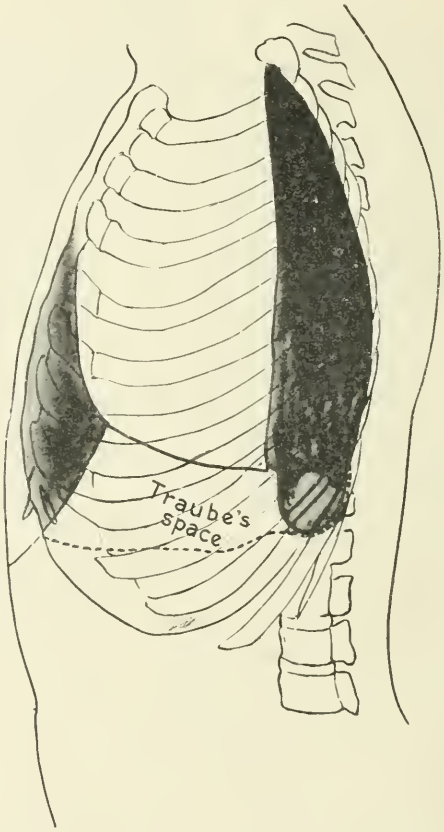

FIG. 8.—Diagrammatic illustration (lateral view) of a left-sided pleurisy with effusion, having a vertical column of exudate located in the posterior portion of the upright chest. Note the absence of encroachment upon Traube's space and the other contiguous organs with the exception of the spleen, which is displaced downward.

nostic fact, as it helps to differentiate the kind of fluid present within the pleura. For example, nearly all other fluids except purulent, hemorrhagic, etc., are freely mobile. The fluid, either transudate or exudate, having the greatest mobility is that associated with free air in the pleural cavity. A pneumohydrothorax is the most classic example of this variety. Next in order of mobility to a pneumohydrothorax is the transudate of a hydrothorax. The

fluid of a chylothorax (Figs. 9 and 10) is slightly less mobile than that of a hydrothorax, due probably to the character of the fluid and not to the condition of the pleura. The chyle, containing a

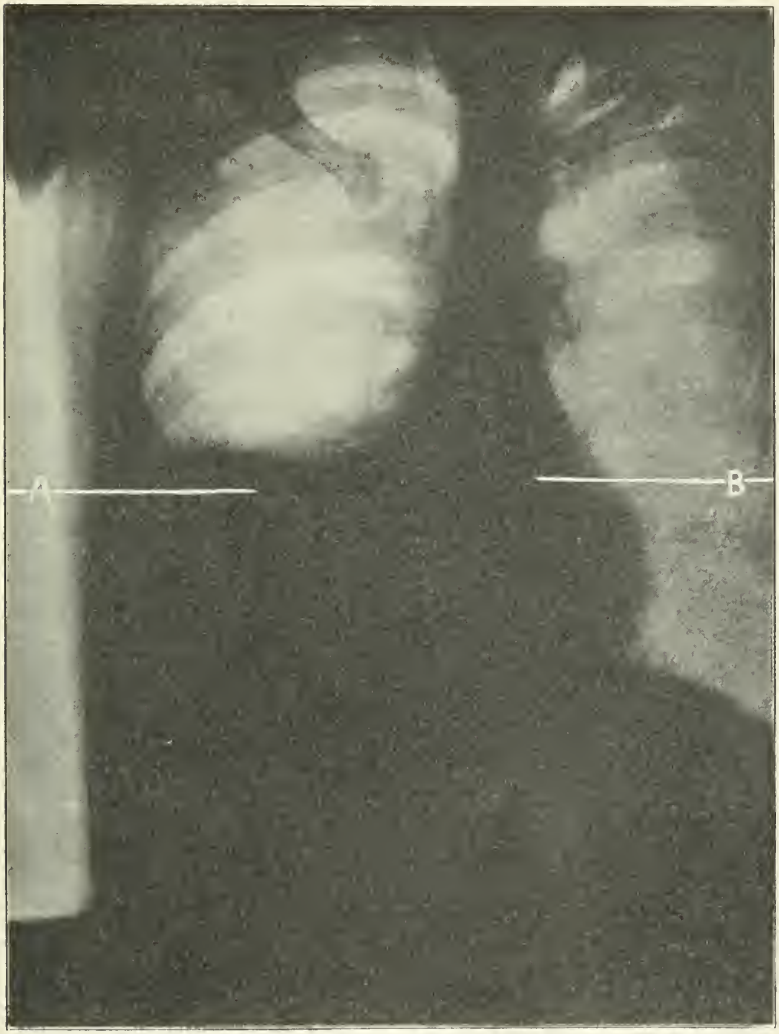

Fig. 9.—Skiagram of chylothorax. (Courtesy of Dr. L. Sale.) Patient in upright position: *A*, fluid shadow (note the upper line, which is nearly horizontal); *B*, heart and vessel shadow.

larger amount of fat, has a greater viscosity than the serous exudate of a hydrothorax. In those pleurisies from which the fluid has been partially withdrawn (Fig. 11), the exudate becomes hydrostatic within its limiting capsule. For instance, in a number of the above

cases after a portion of the effusion was aspirated, the remaining fluid in the pleura was mobile within the limits of the fluid shadow cast before paracentesis. In none of the cases after partial withdrawal did a change of position of the patient affect the lung shadow.

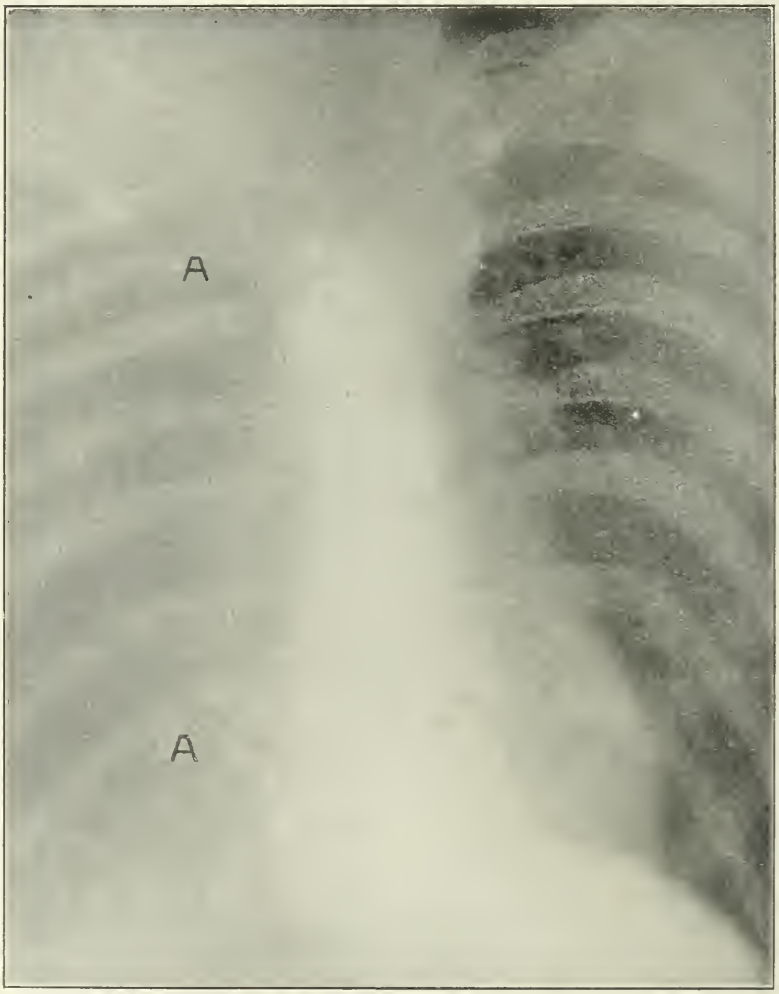

Fig. 10.—Positive skiagram—shadows light instead of dark as in negative. (Courtesy of Dr. L. Sale.) Patient in the horizontal position. Note that the effusion fills the entire right half of the chest, *A*, *A*, and that it is less dense than in Fig. 9, owing to the decreased thickness of the same, due to changed position. These two figures, 9 and 10, illustrate the mobility of the fluid with changed positions of the patient.

Displacement of Organs. A study of the location and mobility of the effusions as has been described above, will explain why all pleurisies with effusions do not cause displacement of organs. This

does take place in those cases in which there is a large exudate in the lower half of the chest, but it is absent in the other cases. This can be seen from a study of the illustrations (Figs. 5, 7, and 8), which demonstrate an absence of marked displacement of the

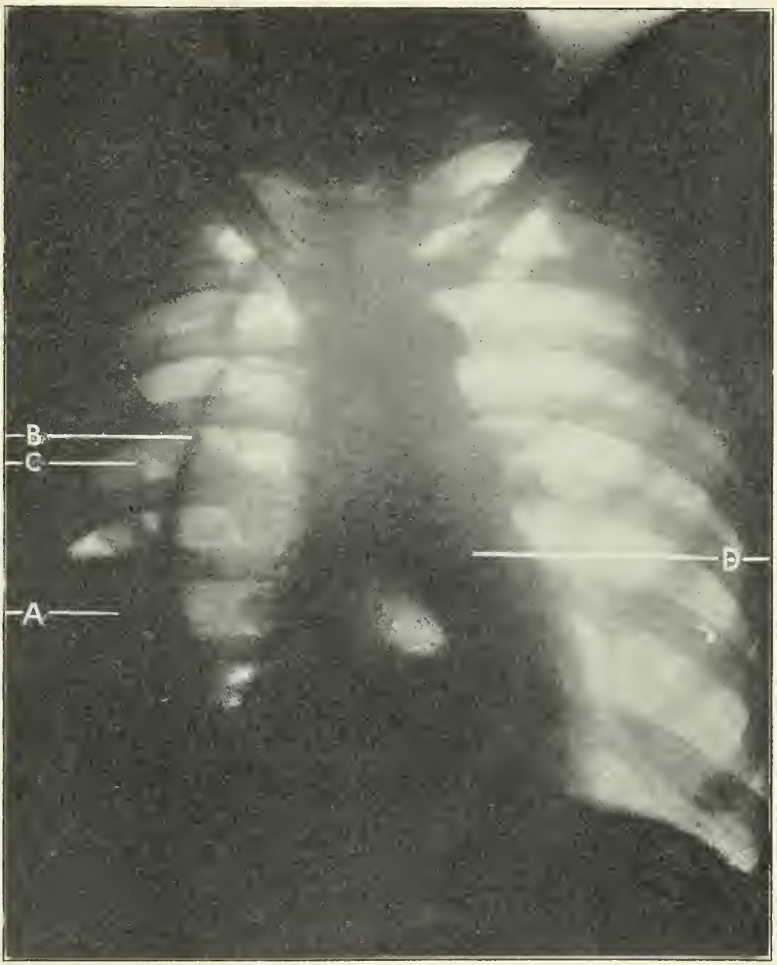

FIG. 11.—Skiagram of right-sided pleurisy with effusion; vertical position of fluid enveloping lateral aspect of lung, in which a portion of the exudate has been removed by aspiration: *A*, fluid shadow; *B*, posterior line of adhesions; *C*, anterior line of adhesions; *D*, heart and blood-vessels.

mediastinum, heart, diaphragm, and other organs. *X*-ray examinations have also demonstrated that in large effusions filling one-half of the chest, there is more displacement of the mediastinum at the centre than at its upper or lower portion. This fact com-

bined with the more or less vertical positions of the fluid explains the absence of Grocco's sign in all those pleurisies with the exception of the ones occupying the lower portion of the upright chest. The displacement of the heart when present is shown by fluoroscopy to be practically that of a displaced heart in its normal axis.

VISCERAL PLEURISY.

Interlobular pleurisy occurs most frequently between the upper and lower lobes of the right lung. This is due probably to the fact that the majority of cases are due to tuberculosis which has a predilection for the upper lobes. A tuberculous lesion of this lobe

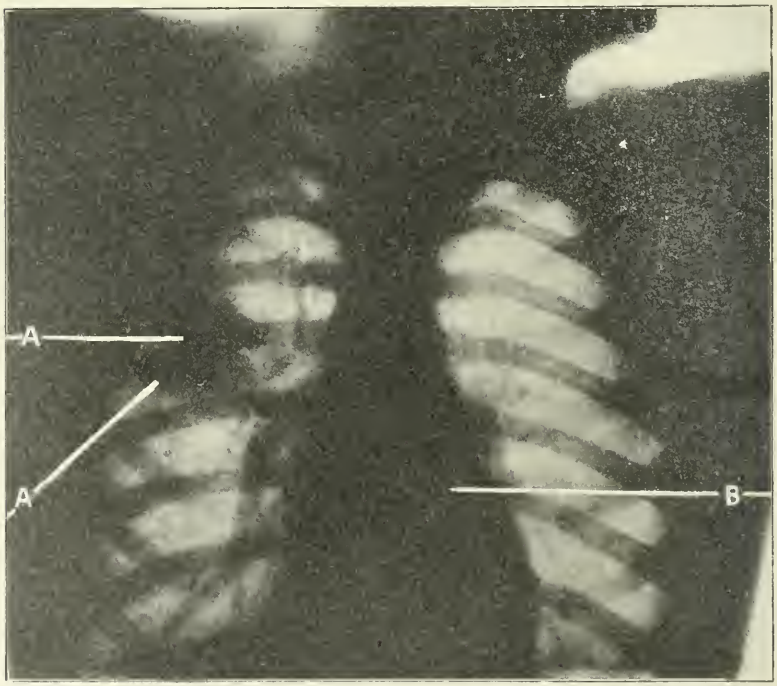

FIG. 12.—Skiagram of interlobular (serous) pleurisy: *A*, fluid shadow of exudate between upper and middle lobe of right lung; *B*, heart and vessel shadow.

extending to the interlobular fissure causes a collection of fluid between the lobes which may or may not reach the thoracic wall. These exudates are very difficult to diagnosticate without the aid of an *x*-ray examination. On the other hand, the diagnosis is comparatively simple with this aid. In this series of cases there were 2 which gave identically the same skiagraph, as is shown in Fig. 12.

In one of the cases the diagnosis of tuberculosis of the upper lobe was made; in the other, a positive diagnosis could not be made on account of the indefinite physical findings. Both cases showed by the skiagraphic and fluoroscopic examination a definite collection of fluid between the upper and middle lobes of the right lung, which was proved by puncture and other clinical evidence to be nonpurulent in character. In these cases paracentesis performed before the fluoroscopic screen is of value in directing the needle into the effusion.

Phrenic Pleurisy. The diagnosis of diaphragmatic and subphrenic collections of fluid has been greatly facilitated by the *x*-ray examination. In all subphrenic conditions, the majority of which are associated with the collection of an exudate below the diaphragm, the diaphragm is projected upward into the thoracic cavity beyond its normal limits. If this projection is extensive, the condition may be recognized by physical examination, but these findings are rarely sufficient upon which to advise radical treatment. On fluoroscopic examination the presence of an immobile diaphragm of normal contour and curve projected above its normal position in the thorax is pathognomic of a subphrenic collection of fluid. Diaphragmatic pleurisy, or a pleurisy between the lower lobe and diaphragm, should be suspected in those cases which produce a fluid shadow in the inferior portion of the chest, obliterating the normal curve and movement of the diaphragm, but not extending to the chest wall.

Conclusions. 1. The location of the fluid in serofibrinous pleurisy is variable. In a great majority of the cases it is more or less in the vertical position in the upright chest. The location is probably dependent upon the most constant position assumed by the patient during the acute stage of the disease. Adhesions forming at this time encapsulate the effusion, fixing it permanently in this portion of the chest.

2. The encapsulation of serofibrinous effusion in different positions of the pleura will explain the discrepancy of the physical findings with relation to the displacement of organs, Grocco's sign, obliteration of Traube's space, mobility with change of position of the chest, and other confusing physical findings.

THE MEIOSTAGMINE REACTION: A CRITICAL REVIEW OF THE LITERATURE, AND A PERSONAL EXPERIENCE WITH THE METHOD.

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A LABORATORY reaction for the diagnosis of malignant disease has been a long-felt want. The subject has interested many workers and numerous different procedures have been elaborated with this end in view. Among these the isohemolytic index has found much favor and is said to give fairly constant results in a large percentage of sera derived from cancer subjects. The glycyltryptophan reaction for gastric carcinoma is another test upon which a large amount of experimentation is being done.

During the last year certain Italian workers, notably, Ascoli and his pupils, have presented a serological reaction based upon certain principles laid down by Ehrlich and also upon some laws of physical chemistry, by means of which they seem able to identify antibodies in the serum of the individual tested, when a specific antigen is employed.

Their procedure consists roughly of extracting the essential principles of the antigen, specific organism or diseased tissue being used, as the case may be, and adding this extract to the serum of the patient to be tested. The surface tension of the mixture is then ascertained. This is measured by the number of drops contained in a certain amount of the fluid, estimated with an instrument of precision, known as the stalagmometer of Traube.*

The mixture is then allowed to incubate at body temperature, and at the end of a definite time the surface tension is again estimated. Should the surface tension be decreased, the number of drops in the same amount of fluid will be increased, that is, the drops have become smaller. In other words, a chemophysical reaction will have occurred.

* The stalagmometer of Traube is merely a very finely and elaborately graduated pipette containing a central bulbous reservoir so as to increase its total capacity to about 8 c.c. The lower, or dropping end of the instrument narrows down to a capillary bore which ends in a flattened ground base about 7 mm. in diameter, on which the solution to be tested accumulates until the drop finally falls, thus insuring uniformity in the size of the drops. The instrument is so graduated that a fraction of a drop can be estimated, and is calibrated so as to contain, when full, a definite number of drops of distilled water at 15° C. The stalagmometer of Traube can be bought from Fritz Kohler, of Leipsic, or C. Gerhardt, of Bonn.

Ascoli claims that if an antigen is incubated with a serum containing specific antibodies this lowering of surface tension will almost always occur, whereas in the absence of a specific antibody the surface tension remains unchanged. He refers to this phenomenon as the meiostagmine reaction (*meion*, small, and *stasso*, drop), because of the fact that the drops have become smaller. He does not attempt to explain the reaction, but claims for it a high degree of specificity. He refers to the specific body in the serum as meiostagmine. Meiostagmine is evidently a body of the first order. It does not need to be activated by another body, as, for example, a complement, although the presence of a complement does not interfere with it. It is not very thermolabile, since it can be heated as high as 56° C. without destroying its activity. The specific bodies in the antigen seem to be lipoids; they are extractable with methyl alcohol and with ether. Nothing more than this is known.

Meiostagmines, according to Ascoli and his pupils, occur in the blood in many diseases. They are present when the body has harbored certain bacteria, such as the typhoid or tubercle bacillus. In the case of the typhoid bacillus their presence is of greater diagnostic worth than that of the agglutinins which form the basis of the Widal reaction, for not only do they make the the diagnosis of typhoid fever certain, but the meiostagmines show no group tendencies, as is true with the agglutinins. Thus, by employing specific antigens of the Eberth bacillus and the Bacillus paratyphosus A or B, these diseases can be clearly differentiated.

In the case of patients infected with the tubercle bacillus, their presence and identification make the diagnosis certain and easy. Experimentally, laboratory animals were infected with human, bovine, and avian types of this bacillus, and in a very few days the presence of human, bovine, and avian tubercle meiostagmines could be made out by the presentation of their respective antigens. Accordingly, this is claimed to be a most accurate way of identification of the various types of the tubercle bacillus.

Following along these same lines, specific meiostagmines were identified in the serum of animals immunized against various substances, such as Witte's peptone, horse serum, etc.

In the case of syphilis, the diagnosis is even more accurate than that hitherto obtained by various complement fixation and deviation tests, such as the Wassermann test, inasmuch as cases of lepra that reacted positively to Wassermann's syphilis test were negative when tested for syphilitic meiostagmines.

Cases of ankylostomiasis and echinococcus showed positive results against their antigens.

In the case of patients suffering from malignant new growths, such as sarcoma or carcinoma, brilliant results were obtained in the identification of specific meiostagmines. In these cases

the investigators were unable to separate carcinomatous from sarcomatous meiostagmines, the serum reacting interchangeably with antigen made of either type of malignant neoplasm. Benign growths, such as fibroma and lipoma, gave negative results against malignant tumor antigens.

Lastly, exudates formed in the pleural, peritoneal, and pericardial cavities in tuberculous and malignant disease when tested against their corresponding antigens gave positive results, the blood serum of the same patients showing no discrepancies in a parallel series of experiments.

These remarkable results show that the reaction has a wide scope of usefulness, inasmuch as it is of service in the diagnosis of many conditions, in some of which the etiological factor is known, in others of which we are at present only upon the threshold of a knowledge of the pathology, as in the case of malignant disease.

This much we will say in a general way as to the rationale and scope of the meiostagmine reaction as presented by Ascoli and his pupils before proceeding to a more detailed analysis of the work reported by them during the last year.

On January 11, 1910, Ascoli's[1] first article on the meiostagmine reaction appeared. He reported a series of experiments in which he tested the sera of typhoid patients against an antigen derived from typhoid bacilli and obtained diagnostic results. His technique was as follows: (*a*) 1 c.c. of serum was obtained in the usual manner, and without inactivation, diluted with 9 volumes of 0.85 per cent. sodium chloride solution. (*b*) The antigen was prepared after the method of Neisser and Shiga,[2] which was as follows: Typhoid bacilli were grown at 37° C. on agar for twenty-four hours, scraped off and emulsified thoroughly in normal saline. This emulsion was then heated in a water bath, kept between 55° and 60° C., for one hour. The emulsion was then reincubated for twenty-four hours at 37° C., and shaken several times during this period. It was then filtered through a Berkefeld porcelain filter and the filtrate used as antigen. Various dilutions of antigens were tested, ranging between 1 to 100 and 1 to 100,000, normal saline being used as diluent. (*c*) Method of mixing: 9 c.c. of diluted serum was added to 1 c.c. of the various dilutions of antigen and incubated at 37° C. for two hours. (*d*) Method of counting: The number of drops contained in a definite amount of this mixture was ascertained by means of Traube's[3] stalagmometer before and after incubation, the latter counting being done after the fluid had regained room temperature.

His results showed that when serum and 1 per cent. antigen were employed as above described there was an increase of 3.2 drops after incubation as compared with the count before incubation, providing a specific serum and antigen had been employed. Greater dilutions of antigen gave less than 2 drops' increase, while sodium

chloride as antigen gave only 1 drop difference. A control with normal serum and typhoid extract gave an increase up to 1 drop.

He concludes from the above that a difference of 2 or more drops warrants a diagnosis of typhoid fever.

In attempting to arrive at a conclusion as to the nature of the specific endobody in the typhoid bacillus that was playing an active role in the reaction, he tried variously modified antigens and found: (1) That the reaction occurred with an alcoholic extract of the evaporated filtrate of the Neisser-Shiga emulsion. (2) He now added alcohol to the Neisser-Shiga salt solution antigen, and a precipitate occurred. This was filtered and the filtrate saved. The precipitate was extracted in alcohol and the extract massed with the above-mentioned filtrate. This combination was also active as antigen, but was not as potent as the first. (3) A watery extract of the precipitate mentioned in No. 2 was not potent as antigen.

The next contribution to the subject of the meiostagmine reaction appeared later during the same month by Izar,[4] a co-worker of Ascoli, and discussed the reaction in syphilis. Following Ascoli's technique, he used an extract of 5 grams of dried powdered syphilitic fetal spleen in 50 c.c. of absolute alcohol. This was stirred thoroughly and put into the thermostat for two hours and shaken repeatedly. It was then filtered and the filtrate concentrated to 10 c.c. and diluted as required. Sera were diluted 1 to 20 to 1 to 200, and 9 c.c. was used. Antigen was diluted 1 to 25 to 1 to 100,000, and 1 c.c. was used. It seems immaterial to the end result which strength antigen is used.

His known syphilitic cases gave 2 to 5 drops increase after incubation, whereas the same sera without antigen never showed more than 1 drop increase. Non-syphilitic cases were negative with syphilitic antigen. Two lepra cases with positive Wassermann reactions were negative with this reaction, using syphilitic antigen.

In studying the various organs that would give an antigen for this reaction, he found that alcoholic extract of guinea-pig heart (Landsteiner), alcoholic extract of normal human liver, and artificial extract of Sachs-Bordoni, all gave negative results, and that alcoholic extract of syphilitic liver gave positive results.

During the next month there appeared a contribution by Ascoli and Izar[5] on the meiostagmine reaction in cases of malignant tumors. The antigen used was prepared from rat sarcoma. The tumor was cut up finely and rubbed to a mushy consistency, extracted with 95 per cent. alcohol at 37° C. for twenty-four hours. The alcohol was then decanted and the process of extraction repeated twice more. The sediment was dried at 50° C. and extracted with warm ether three or four times in twenty-four hours. The ether was decanted and the sediment again extracted,

with alcohol, until the fluid was colorless. All the decants were then massed and dried at 50° C. From the residue a saturated ether extract was made.

Before using it the antigen was diluted 1 to 10 to 1 to 500 with 0.85 per cent. saline solution. Sera to be tested were diluted 1 to 20

The serum of rats with sarcoma gave $4\frac{1}{2}$ to 8 drops increase, whereas normal rat serum gave at most $1\frac{1}{2}$ drops increase. In 62 cases of malignant newgrowth he obtained 58 positive reactions. Of 48 controls, all were negative. With an antigen derived from human carcinoma he found an increase of from 4 to 8 drops, but had to use antigen in dilutions of 1 to 10,000, as lower dilutions, strange to say, gave positive reactions with normal sera. The number of cases thus tested is not mentioned.

The next publication appeared March 12, 1910, by Izar and Usuelli.[6] This is a more extensive article, dealing with many points of laboratory technique which he considers necessary in order to obtain results. He makes the following statements: (1) The serum of the patient should be diluted with 0.85 per cent. salt solution. (2) First count the diluted serum alone, then add the antigen and incubate for two hours at 37° C. or for one hour at 50° C. (3) Remove and count the mixture, but only after it has been thoroughly cooled to room temperature. (4) It is imperative to determine the proper strength of antigen. (5) Antigen dilutions should be thoroughly emulsified. This is best done by placing the spirituous antigen in a tube and then adding the diluent all at once and shaking. (6) An increase of 2 or more drops is a positive reaction. (7) Sera may be kept a long time (not indefinitely however) in a cool place without much deterioration. (8) Alcoholic extract of guinea-pig heart and normal human liver, declared in a previous article to be worthless as a syphilitic antigen, he has found to be available. (9) Human sera of malignant disease and of mice and rats infected with carcinoma and sarcoma were tested against all three varieties of antigen (human malignant tumor, rodent carcinoma, and rodent sarcoma antigens), and found to react with all, but better when the homologous antigen was used.

In cases tested he obtained the following results: Ninety cases of syphilis gave 67 positive reactions; 18 cases of doubtful syphilis gave 8 positive reactions; 104 cases not infected with syphilis gave only 2 positive results against syphilitic antigen.

The next publication was by Izar,[7] in which he discussed the reaction in typhoid, tuberculosis, echinococcus disease and ankylostomiasis. Here a slight variation from the serum technique is mentioned, 15 to 20 drops of blood in distilled water being used instead of serum. The incubation period is also modified, leaving it to the discretion of the experimenter whether he shall

incubate for two hours at 37° C., or one hour at 50° C., or two hours between 30° and 50° C., in the last case replacing the fluid evaporated with distilled water. Stock antigen, he says, can be kept long periods of time, but not indefinitely. Diluted antigen, however, will last hardly forty-eight hours.

In testing tuberculous cases, he found that of 40 cases of advanced tuberculosis, 39 were positive, whereas the controls were universally negative. In typhoid fever cases, 9 cases with positive Widal reactions, were all positive. In ankylostoma, of 6 cases, all were positive. In 11 cases of echinococcus disease all were positive.

Shortly after this Ascoli and Izar[8] reported upon the meiostagmine reaction in sera obtained from animals immunized against Witte's peptone, gelatin, and horse serum, using these substances respectively as antigens, and found the reactions of their sera positive and specific.

About the same time D'Este[9] reported from the surgical clinic of Professor Pausini, at Pavia, on the meiostagmine reaction in surgical conditions. In 15 cases of surgical tuberculosis where the diagnosis was controlled by operation his tests showed 1 to $2\frac{1}{2}$ drops increase. In 4 cases of pulmonary tuberculosis, all of which showed tubercle bacilli in the sputum, he obtained $1\frac{3}{10}$ to 3 drops increase. In testing 11 normal sera against tubercle bacillus antigen, he obtained not more than $1\frac{1}{10}$ drops increase.

In working with the sera of cases of malignant disease he found that in 12 cases (11 of which were operated upon) he obtained 1 to 3 drops increase. In 10 non-malignant neoplasms (8 of which were operated upon) he obtained negative results in all against malignant tumor antigen.

On May 24, 1910, Micheli and Cattoretti,[11] pupils of Ascoli, added the following data to the reports of the meiostagmine reaction: (1) The active elements of tumors employed in the reaction as antigen are lipoids and are thermolabile. (2) Not every specimen of malignant tumor will give extractile bodies that can be used as reagents. (3) Every antigen should be titrated so that one would be using the weakest solution that would produce 1 to $1\frac{1}{2}$ drops increase against a normal serum. (4) Antigen in stronger concentration than the above is meiostagmine positive with normal sera. (5) The active elements in the sera of tumor cases are different from all other previously known antibodies in that they are relatively thermostabile and have a peculiar reaction to ether as a reagent.

Two months later, Verson,[13] of Turin University, reported on a series of cases, verifying some of Ascoli's results, though not having quite as high a percentage of positive findings. Ten of 18 malignant tumors gave positive tests; 6 non-malignant cases were negative.

In testing sera derived from 3 cases of malignant disease against an antigen made from colloid goitre, he obtained a positive meiostagmine reaction in all 3 cases, whereas, of 2 goitre patients, only 1 gave a positive reaction. Normal sera were negative against this antigen. Extract of tuberculous lymph nodes was not satisfactory as anitgen against tuberculous cases.

In August, 1910, Stabilini,[14] from Pansini's clinic, working along the same lines as D'Este, reports: In 32 cases of malignant tumors, 10 of which had only clinical diagnoses, he found $2\frac{1}{10}$ to 3 drops increase. One case of carcinoma mammæ gave 7 drops increase, while 1 case of carcinoma ventriculi, proved microscopically, gave an increase of but $\frac{7}{10}$ drop. One case clinically diagnosticated as sarcoma of the thigh had only $1\frac{4}{10}$ drops increase. In 27 cases of non-malignant tumors and other conditions the results never showed an increase of more than $1\frac{1}{10}$ drops. He considers $1\frac{1}{2}$ to 2 drops increase as only suspicious.

At the same time, Gasharrini,[15] a pupil of Izar, studied the reaction in experimental tuberculosis and found that the sera of rabbits and guinea-pigs infected with human, bovine, and avian types of tubercle bacilli were meiostagmine positive against their homologous antigens only. The sera gave positive reactions four to five days after injection. He considers the test accurate enough to be used in differentiating the various types of tubercle bacilli.

Vigano,[16] a pupil of Ascoli, reported on the reaction in 6 typhoid cases. He obtained positive reactions in all with typhoid antigen, but negative readings with paratyphoid A and B antigens.

Gasharrini,[17] from Ascoli's laboratory, reported upon results obtained in testing various serous exudates for meiostagmines. In all, 25 fluids were tested: 4 pleural tuberculosis fluids and 2 peritoneal tuberculosis fluids were positive with tubercle antigen; 4 pleural exudates, 3 peritoneal exudates, 1 hydrothorax, 1 peritoneal transudate, and 1 pericardial fluid, all from cases of malignant disease, gave positive reactions against malignant tumor antigen; 5 idiopathic pleurisies not proved to be tuberculous were negative against tubercle antigen, while 4 exudates from non-malignant cases were negative against tumor antigen. In tests made upon the blood of all but 4 of the 25 cases, no discrepancies occurred when compared with the results upon the exudates.

The above historical review covers ten months, during which time the results reported were universally satisfactory. At this point, in an article published October 11, 1910, Ascoli and Izar[18] advocate certain changes in the technique of the reaction. They advocate a change in the preparation of antigen, which is indeed much simpler than that previously employed. They cut the tumor into fine pieces, dry in vacuo, pulverize the tumor, and treat 0.5 gram of the powder with 25 c.c. of methyl alcohol, at 50° C., in a closed vessel, for twenty-four hours, shaking from

time to time. Filter warm, allow the filtrate to cool, and then filter again (Schleicher and Schull 590 filter paper). Titrate. The titer, they say, lies mostly between 1 to 100 and 1 to 200, that is, 1 c.c. of a 1 to 100 or 1 to 200 watery emulsion of this methyl alcohol antigen should be used to 9 c.c. of serum diluted 1 to 20 with 0.85 per cent. sodium chloride. The antigen should never be shaken. Always have a positive and a negative control serum. The best positive control is a mildly positive serum. The serum to be tested can be preserved with 0.4 per cent. carbolic acid without interfering with the reaction. In order to make the test they proceed as follows: To 9 c.c. of serum diluted 1 to 20 with saline is added 1 c.c. of distilled water and counted before and after incubating for one hour at 50° C. This is used as a control. To 9 c.c. of serum diluted 1 to 20 with saline is added 1 c.c. of antigen emulsion of the desired strength. This is counted only after incubation for one hour at 50° C. The fluid after being taken from the incubator should be cooled to room temperature very gradually. If done hastily the reaction is rendered worthless.

Izar,[19] writing on the properties of tumor lipoids (an experimental study), states that the sera of rats in which transplantation of rat sarcoma had failed were meiostagmine negative. That in a guinea-pig in which he had transplanted rat sarcoma, he was able to demonstrate a sarcoma meiostagmine as long as the tumor remained. As soon as it became completely absorbed the guinea-pig became meiostagmine negative. That the injection of rat sarcoma antigen into rats or guinea-pigs makes their sera meiostagmine positive.

A. Ascoli[20] tested the reaction in the foot and mouth disease of cattle, and found 22 of 28 cases positive, whereas, of 36 non-infected animals, only 2 gave an increase of more than 1 drop.

In November, 1910, Micheli and Cattoretti,[21] in attempting to verify the results of Ascoli, reported: In 27 malignant neoplasms the sera were "more or less" meiostagmine positive. In 4 cases the sera were distinctly negative. In typhoid their results were not in accord with Ascoli's findings. Sera of typhoid immune rabbits gave negative reactions. With syphilitic sera his results were positive against syphilitic antigen, but he also obtained positive results with tumor sera against syphilitic antigen. A great number of tuberculosis cases in his hands gave the reaction against tubercle antigen.

Kelling,[22] in January, 1911, in testing Ascoli's method, found in 45 cases of malignant growths positive results in but 21 (47 per cent.), even though he considers an increase of $1\frac{1}{2}$ drops as a positive reaction.

During the Thirty-ninth Surgical Congress, held at Berlin in March, 1910, at which Ascoli spoke concerning his results, Stuber, of Berlin, reported that at Bier's clinic they were unable to obtain

any results with the meiostagmine reaction in undoubted cases of malignant growth, even against imported Italian antigen. They had had similar negative results with antigen made from native animal tumors.

Other articles appeared during this time, but embodied nothing new, and are, therefore, only referred to in the tabulated literature.

In looking over the entire field covered by these workers, as recorded in the above literature, one cannot fail to observe the following facts:

Although the results obtained in the first article were all that could be desired, yet a radical change in technique was instituted in the reports that followed.

In the first article the serum antigen mixture was counted before and after incubation, while in the articles that followed the serum alone was counted, and the antigen having been added, the mixture was incubated and again counted. The increase in the number of drops ascertained by the difference in these counts was used for the diagnosis. We see no logical reason for this change; in fact, we consider the original technique only as correct from a serological standpoint.

Further, a discrepancy was noted in the preparation of syphilitic antigen. Izar[4] makes the statement that guinea-pig heart and normal human liver were worthless as antigen, whereas six weeks later he[6] states positively that they can be used very well as antigen, and gives no explanation why he changed his opinion.

Again, for no apparent reason, the diluent of the antigen is changed from normal saline to distilled water, while the diluent of the serum remains unchanged.

Izar[4] states that syphilitic antigen can be used in any dilution from 1 to 25 to 1 to 100,000—rather a remarkably wide range—and yet in a subsequent article he[6] draws special attention to the necessity of absolute titration. Again, while $\frac{n}{1000}$ acetic acid used as a diluent of sera is said by Ascoli[8] to increase the activity of antigen remarkably (2 to 5 drops), yet strange to say, this desirable modification is not employed in any of his subsequent work.

Although all the work done seems to point to the absolute specificity of the reaction in malignant disease, and in spite of the fact that Micheli and Cattoretti[11] found that not all malignant tumors were of value in antigen manufacture, yet Verson[13] was able to get positive results with colloid goitre antigen against sera of malignant disease.

Aside from these changes in technique, it is a matter of surprise to note the apparent lack of interest displayed in medical centres other than those of Italy in this simply performed reaction, which is of such vast importance clinically.

While these articles were appearing, we made tests in the pathological laboratory of Mount Sinai Hospital, introducing, as they appeared, the changes in technique brought out by the Italian

investigators. We have never attained what we have considered to be a positive result. We submit the following protocols.

The first tests were made in an attempt to verify the reaction as a diagnostic aid in typhoid fever. As antigen, an extract of typhoid bacilli was prepared after the method of Neisser and Shiga.[2] The serum was obtained from 4 typhoid suspect cases:

	Agglutination.	
Case I, E. F.	Widal negative.	No blood culture.
Case II, S. R.	Widal positive.	No blood culture.
Case III, F. G.	Widal positive.	Blood culture showed typhoid bacillus.
Case IV, J. P.	Widal negative.	No blood culture.

Technique: Antigen, 1 to 500 dilution in 0.85 per cent. NaCl solution, 1 c.c. used. Serum, 1 to 10 dilution in 0.85 per cent. NaCl solution, 9 c.c. used. Incubated at 37° C. for two hours.

	Count before incubation.	Count after incubation.
Case I	46	47
Case II	46	46 + 10
Case III	46 + 2	46 + 15
Case IV	46 + 15	47 + 5
NaCl (control)	47 + 5	48 + 5

Following this a cross-test was made using a known typhoid serum, a known syphilitic serum, a typhoid antigen, and a syphilitic antigen. The known typhoid serum was from Case III of the previous list. The syphilitic serum gave a strongly positive Wassermann reaction. The typhoid antigen was that used in the previous experiment. The syphilitic antigen used was the acetone insoluble fraction obtained from a congenital syphilitic liver dissolved in methyl alcohol. Of this, 1 c.c. of a 1 to 25 dilution in normal saline was used.

	Before.	After.
Typhoid serum, 1 to 10, 9 c.c. 1. Typhoid antigen, 1 to 100, 1 c.c.	47 + 5	48 + 5
Typhoid serum, 1 to 10, 9 c.c. 2. Syphilitic antigen, 1 to 25, 1 c.c.	47 + 5	48 + 5
Syphilitic serum, 1 to 50, 9 c.c. 3. Syphilitic antigen, 1 to 25, 1 c.c.	47 + 5	47 + 5
Syphilitic serum, 1 to 50, 9 c.c. 4. Typhoid antigen, 1 to 100, 1 c.c.	47	46 + 5
5. NaCl, 0.85 per cent., 10 c.c.	45 + 5	46 + 5

The Reaction in Malignant Tumors. The antigen used was prepared according to the method set forth by Ascoli and Izar.[5] The material used consisted of: (1) A round-celled sarcoma of the foot, diagnosticated microscopically. This will be referred to as "Antigen Sarcoma A." (2) A carcinoma of the breast, diagnosticated microscopically. This will be referred to as "Antigen Carcinoma B."

The sera used were obtained from the following patients:

Case I.—L. R. Clinical diagnosis was sarcoma of femur. Autopsy showed an embolic aneurysm of the femoral artery with malignant endocarditis.

Case II.—A. S. Clinical diagnosis was carcinoma ventriculi, with liver metastases.

Case III.—I. K. Clinical diagnosis was carcinoma ventriculi. Exploratory laparotomy, which showed a large inoperable tumor of the stomach.

Case IV.—S. S. Neoplasm of lung. Fluid withdrawn from chest showed sarcoma cells. Patient developed spinal metastases.

These sera were tested against both Sarcoma A and Carcinoma B antigen, with the following results, the serum being diluted 1 to 20 and the antigen 1 to 500.

Sarcoma Antigen A.

	Before.	After.
Case I	53	53 + 3
Case II	53 + 4	54 + 5
Case III	53 + 6	54 + 5
Case IV	53 + 2	54 + 5

Carcinoma Antigen B.

	Before.	After.
Case I	53 + 16	53 + 4
Case II	53 + 12	54 + 4
Case III	53 + 2	54 + 2
Case IV	53 + 5	54 + 1

Thus far no positive results were obtained in dilutions of antigen as recommended by Ascoli and his pupils, and inasmuch as the serum dilution 1 to 20 was a constant factor in all the experiments reported, we were forced to turn our attention to the antigen as the possible source of error. Granted that the preparation of the antigen was strictly according to the directions laid down, it became then only a question as to what strength one should exhibit in order to obtain satisfactory results.

Our next experiment was made to determine whether Sarcoma A antigen if properly diluted would react to the serum of a known sarcoma case. The serum used was from a case of round- and spindle-celled sarcoma of the femur, proved microscopically.

	Antigen, 1 c.c. in dilution of	Before incubation.	After incubation.
Serum, 9 c.c. diluted, 1 to 20	1 to 10	55 + 5	57
	1 to 50	53 + 8	54 + 4
	1 to 100	52 + 16	53 + 16
	1 to 250	52 + 8	53 + 12
	1 to 500	53 + 7	53 + 8
	NaCl control	52 + 9	53 + 8

Incubated in water bath two hours at 37° C. Receptacles being covered to prevent evaporation.

Similarly to the above, Carcinoma B antigen was tested against the serum obtained from a patient suffering from carcinoma of the rectum, recurrent after operation, and proved microscopically to be an adenocarcinoma with involvement of the lymph nodes.

	Antigen, 1 c.c. in dilution of	Before incubation.	After incubation.
Serum, 9 c.c. diluted, 1 to 20	1 to 10	54 + 8	55
	1 to 50	52 + 18	53 + 3
	1 to 100	53 + 2	53
	1 to 250	52 + 10	54
	1 to 500	53 + 3	52 + 18
	NaCl control	52 + 8	54 + 12

Having obtained no results with these antigens, other antigens were made.

Antigen Carcinoma C was obtained from a carcinoma mammæ medullare, and tested against the serum of a patient suffering from a carcinoma of the gall-bladder. The gall-bladder was only partially removed at the time of operation and the diagnosis substantiated microscopically.

	Antigen, 1 c.c. in dilution of	Before incubation.	After incubation
Serum, 9 c.c. diluted, 1 to 20	1 to 10	51 + 13	52 + 8
	1 to 50	51 + 12	51 + 14
	1 to 100	51 + 12	52 + 16
	1 to 250	51 + 7	52 + 18
	1 to 500	51 + 5	53 + 3
	NaCl control	51 + 10	52 + 13

The next antigen was made from rat sarcoma, furnished through the kindness of Dr. Richard Weil, and labelled Sarcoma Antigen D, and tested against a known case of sarcoma of the femur proved microscopically.

	Antigen, 1 c.c. in dilution of	Before incubation.	After incubation.
Serum, 9 c.c. diluted, 1 to 20	1 to 10	61 + 10	62 + 2
	1 to 100	51 + 2	52 + 2
	1 to 500	51 + 12	52

In the meantime Ascoli[18] had modified his preparation of antigen, and hoping to obtain results with this newer technique of antigen preparation, we proceeded with antigens E and F.

Antigen E was made from a carcinoma proved microscopically, and was tested against the serum of a patient clinically suffering with a carcinoma of the esophagus.

	Antigen, 1 c.c. in dilution of	Before incubation.	After incubation.
Serum, 9 c.c. diluted, 1 to 20	1 to 10	60 +10	63 +16
	1 to 50	53 +10	54
	1 to 100	52 +11	53 +10
	1 to 250	52 +10	53 + 6
	1 to 500	52 +15	53
	NaCl control	52 + 5	53 +10

Incubated for one hour at 50° C. and allowed to cool to room temperature for thirty minutes before second count was made.

The same antigen was tried against the serum of a case of carcinoma mammæ, with the following results:

	Antigen, 1 c.c. in dilution of	Before incubation.	After incubation.
Serum, 9 c.c. diluted, 1 to 20	1 to 10	57 +8	60
	1 to 50	52 +5	54 +10
	1 to 100	52	54
	1 to 250	52 +8	53 +14
	1 to 500	52	54
	NaCl control	52 +4	54 +10

The dilution 1 to 10 might on casual inspection appear to be a positive test, but the control forces us to disregard it.

Antigen F was prepared from a medullary carcinoma mammæ, according to the new method, and was tested against a case of carcinoma ventriculi, diagnosticated clinically and verified by exploratory laparotomy.

	Antigen, 1 c.c. in dilution of	Before incubation.	After incubation.
Serum, 9 c.c. diluted, 1 to 20	1 to 10	67 +17	62 +17
	1 to 100	54	52 + 5
	NaCl control	51 +14	52 +8

Incubated at 50° C. for one hour and cooled to room temperature before the second count was made. Evaporation prevented.

The same antigen was tested against an inoperable carcinoma of the rectum on whom a colostomy had been done.

	Antigen, 1 c.c. in dilution of	Before incubation.	After incubation.
Serum, 9 c.c. diluted, 1 to 20	1 to 10	55 + 3	66 +10
	1 to 100	52 +18	52 + 5
	NaCl control	52	52

In the last few protocols the use of a strong antigen dilution seems to give marked differences before and after incubation, but these are to be disregarded, since all investigators agree that antigen when used in dilution less than 1 to 50 gives unreliable results and may react strongly positive with normal sera. From a study of the above tables we must conclude that the meiostagmine reaction in our hands has not proved satisfactory as a diagnostic aid.

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THE TREATMENT OF BRONCHIAL ASTHMA.

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It is not my purpose to enumerate a catalogue of drugs, but to review briefly those agents which have seemed of most value in a series of cases seen by my colleagues and myself in the Touro clinic in the last couple of years.

In some 7000 patients we have seen 31 cases of bronchial asthma. Of these 31, 8 were white males and 6 white females, a total of 14 whites; 8 were negro males and 9 negro females, a total of 17 negroes. As the clinic is very nearly evenly divided between whites and negroes (a recent summary showing about 45 per cent. white and 55 per cent. negroes) there is no apparent difference in the incidence between whites and negroes. The same is true of the

comparison between the sexes, for the asthmatics were 16 males and 15 females respectively, and the clinic attendance again is approximately equally divided between males and females. So far, then, as our experience goes there is nothing in sex or race that enters as a factor into predisposition or causation or calls for consideration in discussing causal treatment.

We may conveniently adopt the usual plan and discuss separately the treatment of the attacks and the treatment of the intervals. The drug that will give the surest relief in an attack is the drug which we should reach for last, namely, morphine. The distress of a paroxysm is so great, the relief by morphine so complete and so sweet, and the occasion for the use of the hypodermic arises so repeatedly, that it is almost certain that we shall create a habit. Morphine, therefore, should be a last resort. Much safer, but also much less sure, is the action of atropine. Where it is successful its effect is probably to be attributed to its antispasmodic influence on the terminal nerve endings, causing a relaxation of the contracted musculature of the bronchi. In a relatively few cases nitroglycerin, by hypodermic, affords relief. These are probably cases where the blood pressure is high. Other means of relaxing the bronchial spasm have sometimes proved useful in our hands. Some of our patients have obtained scant comfort from smoking cigarettes of stramonium leaves or inhaling the fumes of burning stramonium leaves, nitre, etc. Perhaps the most efficacious drug next to morphine is adrenalin chloride. Where it succeeds its action is nothing short of marvellous. Hardly have the 10 to 15 drops of the 1 to 1000 solution been given under or into the skin when the patient will declare that he is already better. In fact, it has been my repeated experience that the relief begins before the hypodermic needle can be withdrawn.

In view of the fact that nitroglycerin and the nitrites are supposed to relieve asthma by their vasodilator and blood pressure reducing effects, while adrenalin is generally accounted a vasocontractor and augmenter of blood pressure, I have been interested in observing the blood pressure during asthmatic paroxysms, before and after the administration of adrenalin by hypodermic. In general, it may be stated that these hypodermics of adrenalin have had practically no effect upon the blood pressure. In some instances, in fact in most instances, the blood pressure is lowered about 5 mm. and returns within a few minutes to its original level. This action is the same whether symptomatic relief is obtained or not. The blood pressure of asthmatics in paroxysms as observed by me was not, as a rule, high; most frequently it was from 100 to 125 mm. of mercury and in one patient as low as 90 mm. In one patient the initial blood pressure was 165, which fell after the hypodermic to 148. There was no relief in this case. I give below some of the observations:

Case I.—No. 6119. C. H., white, male, aged forty-two years. 11.30 A.M., blood pressure, 105; 11.30 A.M., adrenalin, minims, 10 (1 to 1000), hypodermically; 11.32 A.M., blood pressure, 98; 11.32 A.M., much easier; 11.33 A.M., blood pressure, 100; 11.39 A.M., blood pressure, 100; 11.43 A.M., blood pressure, 98; 11.48 A.M., blood pressure, 100; 11.56 A.M., blood pressure, 100.

Case II.—No. 4620. N. H., colored, male, aged twenty-six years. 10.20 A.M., blood pressure, 148; 10.20 A.M., adrenalin, minims, 10 (1 to 1000), hypodermically; 10.23 A.M., blood pressure, 165; 10.26 A.M., blood pressure, 150; 10.28 A.M., blood pressure, 148; 10.35 A.M., blood pressure, 148, no relief.

Case III.—No. 5470. E. J., colored, male, aged twenty-five years. 10.25 A.M., blood pressure, 130; 10.25 A.M., adrenalin, minims, 15 (1 to 1000), hypodermically; 10.25 A.M., better; 10.26 A.M., blood pressure, 125; 10.27 A.M., blood pressure, 125, much better; 10.29 A.M., blood pressure, 122; 10.31 A.M., blood pressure, 122; 10.34 A.M., blood pressure, 128; 10.35 A.M., blood pressure, 127; 10.36 A.M., blood pressure, 130; 10.37 A.M., blood pressure, 130; 10.39 A.M., blood pressure, 130; 10.40 A.M., blood pressure, 130.

Case IV.—No. 5044. L. B., white, male, aged forty years. 10.32 A.M., blood pressure, 90; 10.32 A.M., adrenalin, minims, 15 (1 to 1000), hypodermically; 10.32½ A.M., great deal easier; 10.33 A.M., blood pressure, 90; 10.33½ A.M., greatdeal better; 10.35 A.M., blood pressure, 90; 10.36 A.M., marked relief; 10.38 A.M., blood pressure, 90; 10.41 A.M., blood pressure, 95; 10.48 A.M., blood pressure, 93.

Case V.—No. 6063. F. P., white, male, aged forty-eight years. 11.02 A.M., blood pressure, 115; 11.03 A.M., adrenalin, minims, 10 (1 to 1000), hypodermically; 11.04 A.M., little better; 11.05 A.M., blood pressure, 110; 11.07 A.M., breathing easier; 11.09 A.M., blood pressure, 115; 11.22 A.M., blood pressure, 115.

Case VI.—No. 4178. C. B., colored, female, aged twenty-eight years. Experiment by Dr. C. L. Eshleman. Ten minutes after hypodermic injection of adrenalin, minims, 10, the blood pressure went from 125 to 140. Slight, but not marked relief from wheezing was obtained.

I wish to be emphatic, however, in saying that while our results have been usually gratifying, still we have not been without our failures.

Another point worthy of notice is that the sibilant and sonorous rales were not banished coincidently with the relief of the paroxysm. If we assume, as I think is most plausible, that the adrenalin relieves the spasmodic contracture of the bronchi, then we cannot attribute the production of these rales to this bronchial spasm.

My observations, therefore, are: (1) Blood pressure is not usually high in paroxysms of asthma. (2) Blood pressure is not increased by adrenalin administered hypodermically in such paroxysms, but

tends rather to be lowered. (3) Adrenalin hypodermically frequently relieves the paroxysm, probably by relaxing the bronchial spasm.

This relief is wonderfully rapid. In many cases it is also lasting, and the patients have a rest for longer periods than after being relieved by other means. Other patients find it necessary to demand several such hypodermics in the course of twenty-four hours. One patient, J. M. M., white, male, aged fifty-three years, who had had asthmatic attacks practically daily for six years, and who had tried various inhalants, nitroglycerin and morphine, found the greatest relief and comfort from the adrenalin injections. These he learned to take himself, and used as many as four or five a day, usually at night. If he took the adrenalin in the beginning of the attack he was promptly relieved and expectorated large quantities of thick mucus.

It has been objected that the habitual use of adrenalin will bring about extreme arteriosclerosis, and experimental work, a well as clinical cases with autopsy, have been cited in evidence. To this there are two replies: (1) The frequency of the existence of arteriosclerosis and bronchial asthma in the same individual makes it impossible to say that the arteriosclerosis is due to the administration of adrenalin and not to the usual fundamental cause underlying both the asthma and the arteriosclerosis. (2) Even if it were granted that the adrenalin is responsible for an aggravation of the arterial degeneration still the great relief from misery of attacks more than justifies its use.

Turning now to the treatment of the intervals, we may first take up what may in a certain sense be considered causal treatment. It has been repeatedly pointed out that asthma is a neurosis which has its origin in some point of irritation distant from the bronchi. Such "reflex" points are deflected nasal septa, sensitive points near the inferior turbinates, disordered stomachs, and, in cases of constipation, the intestines. It has comparatively rarely been my experience to trace the attacks to stomach upsets or to constipation; nevertheless, as a possible source of trouble, constipation must be avoided and the dietary must be carefully scanned, especially at the time of the attacks, in order to discover if possible, any article of food which "disagrees." It is also my routine custom to refer all cases of asthma to the rhinologist to determine whether reflex points exist in the nose. In all but a very small percentage of cases the rhinological report has been negative.

An important point in a certain number of asthmatics is the coexistence of obesity. Practically all asthmatics are emphysematous, and when in addition to the increased volume of the lungs there is added the unfavorable conditions for the proper excursions of the diaphragm produced by deposits of fat in the abdomen and in the pendulous abdominal wall, it is easy to understand that the usual chronic bronchitis is unfavorably affected and the predisposition

to attacks correspondingly increased. In some cases, therefore, a suitable reduction cure is indicated. No asthmatic should be permitted to grow fat if it can be prevented.

The sheet anchor in the treatment of bronchial asthma is iodine, usually in the form of potassium iodide. The practically unanimous testimony of patients is that under its administration the paroxysms grow much less frequent and of less severity. It is not necessary to give large doses of the drug, therefore it is usually possible to avoid any disturbance of the stomach. A prolonged course for several months of 10 to 15 grains of potassium iodide, three times daily, should first be given, and therafter these doses should be given for periods of ten days, alternating with ten days of rest. Another favorite prescrption is to direct that the iodide be taken for the first ten days in every month. With either of these methods it is possible to keep up a sufficient saturation with iodine to bring about excellent therapeutic effects without causing any of the undesirable by-effects of iodism. For this reason, my experience with the substitutes for potassium iodide, such as sajodin and the like, is extremely limited in the treatment of this disease.

ASTHMA AND TUBERCULOSIS.[1]

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It is commonly known, though not generally remembered and applied, that asthma and tuberculosis may co-exist in the same patient. The literature upon the subject is unusually scanty. The older writers held that the two diseases were antagonistic. Brügelmann[2] says quite positively that as long as anyone has asthma he cannot become tuberculous.

Hoffmann[3] states that a certain reciprocal exclusion has been assumed to exist between the two diseases, and this, in general, is true. But mistakes in diagnosis will follow if it is applied to the specific case. He also states that when asthma and tuberculosis combine each gives up a part of its peculiarities, the asthmatic attacks becoming weak and indistinct and passing over into indefinite dyspnea, and the tuberculosis degenerating into a fibroid phthisis. This is probably not always true, and is not borne out by the history of one of the following cases.

[1] Read before the Southern Minnesota Medical Association, Rochester, August 3, 1911.

[2] Quoted by Hoffmann.

[3] Nothnagel's Encyclopedia of Practical Medicine, chapter on The Bronchi, p. 241.

The only extensive discussion of the subject, however, that I have been able to find in the literature is in a paper by Soca.[4] This writer makes the startling assertion that he has become convinced from his clinical experience that asthma is always an expression of tuberculosis. He confesses his inability to prove this to the satisfaction of others. Although he cites 700 cases, of which 500 showed the association of tuberculosis either in the individual or the family, he is in a position to report only 200 fairly well-studied cases, of of which number, 70 showed signs which led to a positive clinical diagnosis of tuberculosis in the patient himself. The sputum was not always examined, and the diagnosis was made chiefly upon the history and physical findings. In his experience the tuberculosis followed the asthma in the great majority of the cases. Asthma followed tuberculosis in a small number of cases, while the two diseases very rarely began simultaneously. This paper is not convincing. The conclusions, however, are interesting.

During the last year (August 1, 1910, to August 1, 1911), we have seen in this clinic 82 cases of spasmodic asthma. Of these, 42 cases have been examined personally by the writer. Three of the total number showed positive evidence of tuberculosis and are reported as illustrative cases. During the same time 226 cases of pulmonary tuberculosis were seen.

Case I (a56066).—S. T., male, aged thirty-three years. He had been coughing and wheezing for two years, with frequent attacks of difficult breathing and typical asthmatic seizures. There had been slight loss of weight during the last three months, but no complaint of night sweats or fever.

On examination, the asthmatic type of breathing was present, with spasm of the upper abdominal muscles. Dulness, fine crackles, and squeaks were found over the right infraclavicular and supraclavicular regions. Some dulness was also noted over the area of the left upper lobe. Snores and squeaks could be heard at various places over both lungs. Temperature, 99.5°. The sputum was positive for tubercle bacilli; a second examination corroborated the first. Upon *x*-ray examination infiltration of the left upper lobe and apex was demonstrated. On the right, an interlobar pleurisy between the upper and middle lobes, with infiltration into the upper portion of the lower lobe, was clearly shown (Fig. 1).

Case II (a56250).—E. L. L., male, aged forty-seven years. He had had attacks of cough, shortness of breath, and wheezing for fifteen or twenty years. These attacks were at times spasmodic in character and very severe, particularly in damp weather. They had continued up to the time of examination. There were no data to indicate the period at which the tuberculous process might have begun. This patient was a large, robust man, who

[4] Arch. Gén. de Méd., Paris, 1906, 83, i, p. 1601 to 1610.

worked as a farm hand. He had been told repeatedly that he had asthma, and, what is most important, had doubtless infected many households.

On examination, expansion was limited over the left chest. Inspiration was faint, and expiration blowing over entire left

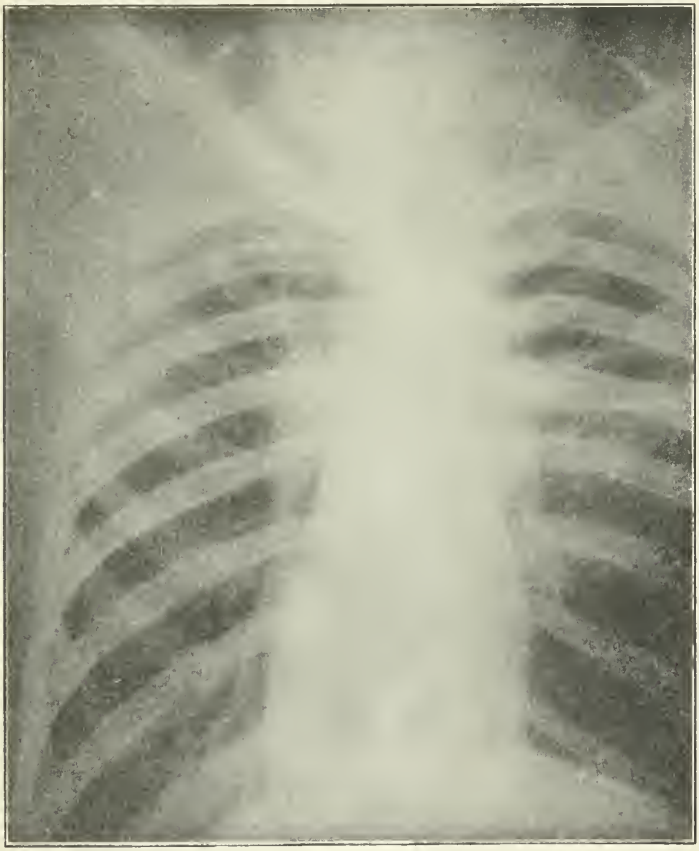

FIG. 1.—The upper left lobe shows considerable infiltration of tuberculous origin. The right chest shows distinctly an interlobar pleurisy between the upper and middle lobes and a diffuse tuberculous process in the middle and upper portion of the lower lobe. Note the appearance and position of the heart; it is elongated and drawn toward the right.

side and the right apex. In addition to whistles and squeaks, which were present quite generally over both lungs, fine, sticky crackles were heard in many places. The sputum was positive for tubercle bacilli. Upon *x*-ray examination the entire left chest showed an extensive thickening of the pleura, with areas of consolidation scattered throughout. The left apex showed more

clearly several consolidated areas. There was also beginning consolidation in the right apex (see Fig. 2).

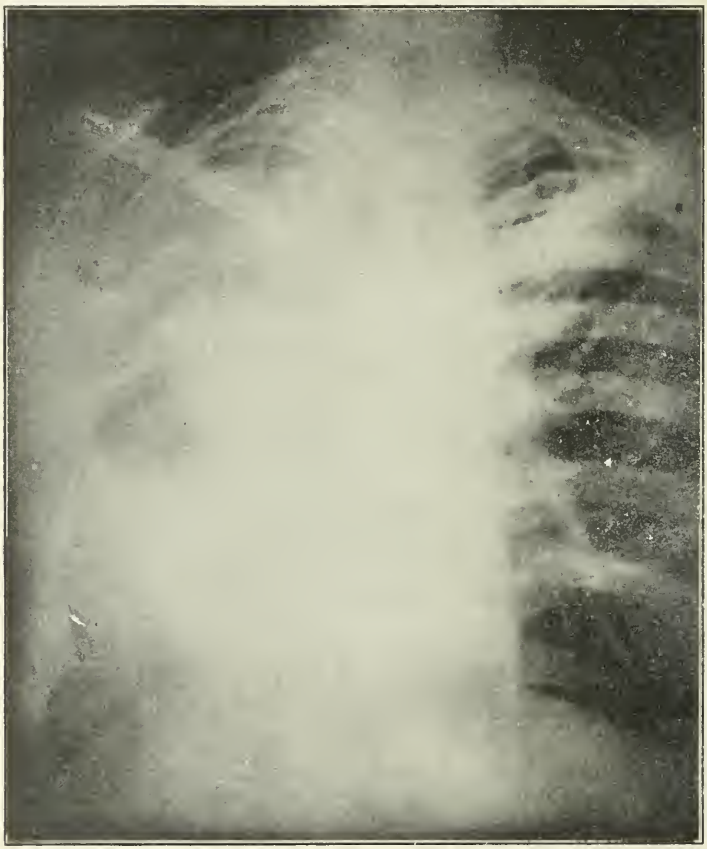

Fig 2.—Shows an extensive thickening of the pleura on the left side from the level of the clavicles to the base. Through this increased area of dulness can be seen scattered areas of consolidation. In the left apex they are seen more clearly. The right apex shows small areas of beginning consolidation and marked thickening of the bronchial tree throughout, with numerous enlarged glands. The heart in this case is drawn strongly to the left; no evidence of its right border being present to the right of the margin of the spine.

Case III (a56247).—Mrs. C. L. B., female, aged thirty years. For two years she had been having asthmatic attacks beginning usually late in the afternoon and continuing until after midnight. These attacks were associated at first with a dry, hard cough without sputum. A year before the examination, fever and night sweats appeared, possibly marking the onset of tuberculosis. Sputum obtained at this time was sometimes bloody. The asthmatic attacks continued however, as before. Several months

previously the patient's condition had been diagnosticated as asthma, but no treatment had been given. Since then the patient's condition had progressed steadily downward. The patient was emaciated and pale, and the right lung was badly affected. Dulness, many fine crackles, and cog-wheel breathing were quite generally

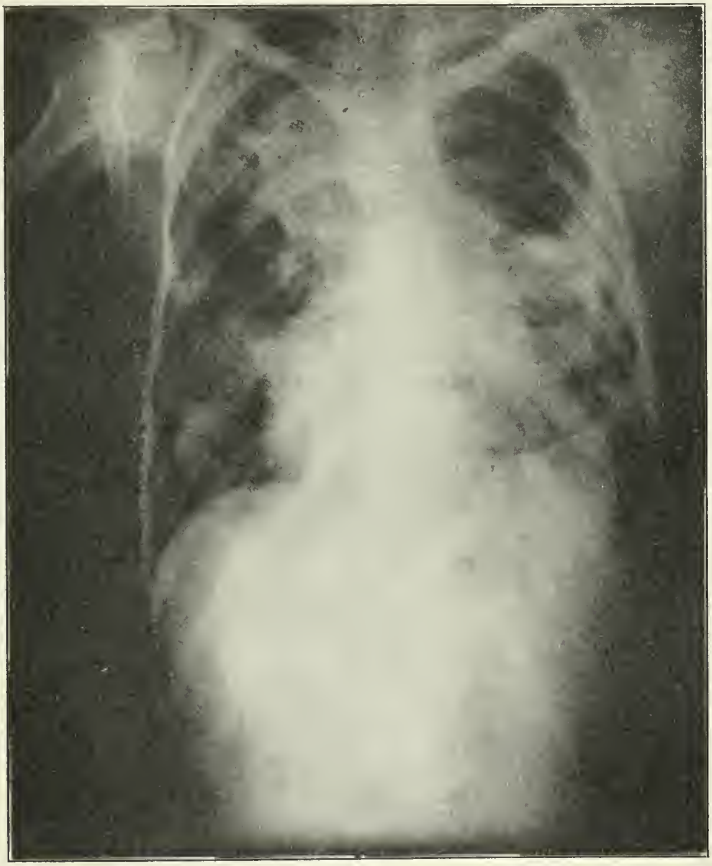

Fig. 3.—The upper right lobe is represented by a huge cavity, several cavities being present in the middle and lower lobe, these lobes being extensively involved by the tuberculous process. The upper left lobe is extensively involved and shows cavity formation. The lower left lobe is also involved to some extent. Note the position of the heart; compare with Fig. 1 and note the similarity. Contrast it with Fig. 2 where the heart is drawn to the left.

present. The left lung was involved, similarly, in smaller areas. Sputum was positive for tubercle bacilli. *X*-ray examination showed apparent absence of the entire right upper lobe. The right middle and lower lobes were extensively involved and showed two or three cavities. The left upper lobe was extensively affected and invasion of the left lower lobe had begun (see Fig. 3).

These 3 cases illustrate the association of asthma with early, advanced, and extensive tuberculosis, respectively. The first case would seem to indicate that the possibility of the occurrence of early tuberculosis with asthma is merely a question of early diagnosis, and in this *x*-ray examination should be of assistance in some cases.

The second patient was a robust, healthy looking, active man, in whom tuberculosis would not be suspected ordinarily, and for this reason he was unconsciously a most effective carrier of the disease.

The third case would suggest that the tuberculous process need not necessarily degenerate into a fibroid phthisis, as Brügelmann and Hoffmann have stated, but may be an acute and rapidly advancing disease even though asthma be present.

In addition to these cases, one patient was observed in whom the radiogram showed a basal pleurisy on the right side which was probably tuberculous. As positive evidence, however, was lacking in this case, it has not been reported in full.

In the diagnosis of asthma, then, it is essential: (1) To examine the sputum carefully and without fail; (2) to avail one's self of the aid of the Röntgen rays, especially if early tuberculosis, on the one hand, or fibroid phthisis on the other, be suspected, for in these the sputum may be negative; (3) to appreciate that the examination of an asthmatic in reality imposes upon the physician the duty of carefully excluding tuberculosis.

PHLEBITIS MIGRANS, WITH REPORT OF A CASE.

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The patient was a widow, aged sixty years, of good family history.

The Past History. There had been three normal labors, the last of which was followed by a right femoral thrombosis. In 1906 a small benign epithelioma appeared on the right leg and has remained without further development. For the last eight years there have been occasional bowel disturbances, attacks of abdominal discomfort rarely amounting to pain, with diarrhea. Between these there is often constipation. A mild osteo-arthritis, involving the small joints of the fingers and the formation of a few Heberdens' nodes, has given some annoyance. A test breakfast in October, 1908, showed hyperchlorhydria, the free hydrochloric acid being 62; the total acid,

104. A Schmidt's test diet, given in May, 1911, showed the digestion of proteid, fat, carbohydrate, and nuclei to be normal.

The Present History. In February, 1909, without obvious cause, the patient suffered a phlebitis of the left calf with pain and slight fever, the process clearing up within three weeks. On October 1, 1909, redness and induration, preceded by pain and tenderness, appeared around a small group of varicose veins in the upper right calf. From this there was complete recovery in a few days. While in Europe in June, 1910, more serious attacks began. For ten days, beginning June 10, the right leg below and above the knee was involved. She was confined in bed for twenty-four days from July 14, with involvement of the right leg and groin, lower abdomen, and left groin, accompanied by fever. On August 19, after severe pain in the left thigh, a process appeared in this region and lasted twenty days. From September 15 the left thigh and knee were involved for ten days, during three of which there was fever. An attack lasting four days, on two of which the temperature was 99.4°, began on October 9, and affected the veins of the left leg below the knee.

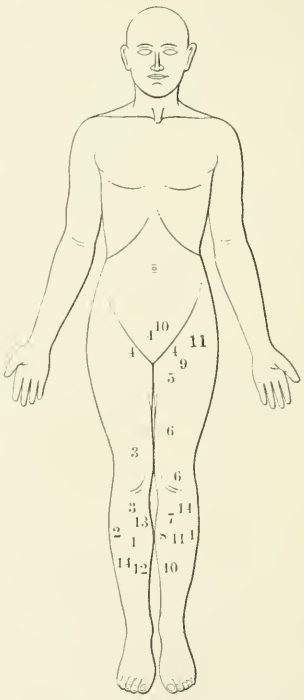
The patient returned from Europe on October 10, 1910, and came under my direct observation. At this time there was a clean tongue, and a normal temperature. The heart and lungs showed nothing abnormal. The arteries were soft; the blood pressure, systolic, 110; diastolic, 75; the pulse rate was 84. The dorsalis pedis and posterior tibial arteries pulsated. Along a superficial vein below the left popliteal space was a small area of redness, tenderness, and induration. There was slight edema of the left leg. Phlebitis appeared October 18, on the inner aspect of the left leg. Nine days later a like process appeared immediately beneath the left Poupart's ligament. On October 28 Dr. J. Gardner Hopkins made a study of the blood. The agglutinating and hemolytic properties of the patient's corpuscles and serum were tested and found normal. The blood culture showed no growth.

A group of epigastric veins and a new group on the inner surface of the left calf were involved by November 3. Another group below the left Poupart's ligament and a small group over the left tibia were affected on November 5 and 13 respectively. On this latter date active treatment, to be described in detail, was begun. On December 20 a process appeared below the right popliteal space; on December 26 another appeared on the inner aspect of the right calf; and on December 28 there were two new "spots," one on the left leg anteriorly six inches below the knee; the other on the right calf. The location and sequence of these attacks may best be followed by reference to the accompanying figure.

The treatment during the attacks had been that of the ordinary thrombophlebitis until November 13, when the true nature of the condition became clear and more successful measures were begun. Thorough sweating in an electric light cabinet for forty-five minutes

at 170° F., twice weekly, massage, active and passive movements to increase both local and general circulation, and the insistence that the condition be ignored by the patient, who was urged to walk, drive, attend concerts, etc., resulted in complete disappearance of the phlebitis within five weeks. There has been no return, and the patient is pursuing her usual life without restrictions.

Thus, we have for study a case in which, within six and one-half months, there were twelve inflammatory processes involving superficial veins of the lower extremities and epigastrium. Each process was preceded by pain in the affected region, lasting from twenty-



Numbers indicate the order in which the phlebitis involved various portions of the body.

four to forty-eight hours, this pain not always being localized exactly at the site of the new lesion. The lesion itself was a superficial, red, hot, tender, indurated area, continuous with the small superficial veins, which were at times more prominent than usual. The size of these areas was variable; the usual width being about three-quarters of an inch, the length varying from one to four inches. Often several branches of a vein were included, so that the process radiated from a common centre. The areas were painful on movement, and there was also spontaneous pain. About some of the processes there was very slight local edema. Infrequently

the slightest degree of edema of the ankle of the affected extremity was observed. Never was there evidence of serious interference with the circulation. Of particular interest is the fact that the process in a given area cleared up within a space of seven to twenty-five days, leaving not the slightest trace of its presence in thrombosis, thickening, or dilatation of the veins, nodulation, edema, or pigmentation. The previously affected vessel could after some of the attacks be seen, and in all respects resembled the contiguous parts of the vein that had not been involved. Systemic symptoms were negligible. I never observed fever, although during some of the attacks in Europe there was slight elevation of temperature. The patient was incapacitated only because of pain on motion, and because she had been thoroughly impressed by her Munich and Paris physicians with the danger of embolism.

Prolonged study of this case furnished several impressions which proved of value in dealing with the condition. It became clear that there was no involvement of the intima of the affected veins, that interference with the blood flow in these vessels was slight, if it existed at all, and that there was never thrombosis. The media, adventitia and perivascular tissues were, therefore, the site of the lesion. Swelling of the outer coats of the veins may have temporarily diminished their caliber, and thus given rise to the slight transient edema occasionally noted. For these reasons the fear of embolism, the chief source of anxiety, could be banished. The paucity of systemic symptoms, the negative blood culture, the absence of any demonstrable portal of entry for microörganisms all spoke against an infectious origin. There was no possibility of trauma being a cause. One is inclined to believe that the etiology lay in some metabolic defect, although such an idea is at best speculative. Somewhat in favor of this view was the accompanying osteoarthritis, a condition supposed by many to be due to faulty metabolism. Toxins produced by such defective metabolism might well exert their greatest influence upon the veins of the lower part of the body where circulation is most sluggish, and where frequent varicosity renders them yet more susceptible. One might consider that the effect in these cases is exerted largely through the vasa vasorum, and less through the intima of the affected vessel. As a working basis in treatment such a conception proved satisfactory.

The literature of phlebitis migrans is meager. In 1903 Ernst Neisser[1] reported a case, and collected 6 others from the literature, all of syphilitic origin. Schwartz,[2] in 1905, described two instances in tuberculous individuals. Both observers examined the lesions microscopically. Neisser found swelling of the outer and middle

[1] Deutsch. med. Wochenschr., 1903, xxix, 37, 660 to 663.
[2] Virch. Archiv f. path. Anat., 1905, clxxxii, 178 to 194.

coats of the vessel from localized cellular infiltration apparently starting about the vasa vasorum; young connective tissue and plasma cells, lymphocytes, many red blood cells, and newly formed bloodvessels making up the new tissue elements. The intima was unchanged and there was no thrombosis. Schwartz found much the same condition, the infiltration differing in that it was somewhat more diffuse than that described by Neisser.

Bennett[3] has called attention to "a condition often mistaken for phlebitis," which from his description I judge to be phlebitis migrans. He emphsizes the uselessness and possible harm of treating these as cases of ordinary thrombophlebitis, advising active, passive, and resisted movements and massage. Blumer[4] describes this form of phlebitis in some detail, remarking that "so far phlebitis migrans has only been observed in connection with syphilis and pulmonary tuberculosis, but as more instances are reported it will probably be shown that it is not invariably associated with these diseases." My own case, in which there was no suggestion of either of these diseases, confirms Blumers' judgment on this point.

Conclusions. There exists a type of migrating phlebitis of toxic origin, the toxin being of either an infectious or metabolic nature, in which the process does not involve the intima; in which there is no thrombosis and slight, if any, interference with the blood flow in the affected veins, in which there is little or no systemic disturbance and which, after a comparatively short interval, heals, leaving no sequelæ. Any of the superficial veins may be involved, the order of frequency being the upper extremities, lower extremities, thoracic wall, and abdominal wall. Although rare, these cases should be recognized, as the treatment differs markedly from that of ordinary phlebitis with its danger of embolism.

My acknowledgements are due Dr. T. C. Janeway, with whom many phases of this case were observed.

CYSTOPYELITIS DUE TO INFECTION BY THE BACILLUS COLI COMMUNIS: ITS SYMPTOMATOLOGY AND DIAGNOSIS.

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Such masters as Lenhartz or F. Mueller openly confessed that until as recently as 1907 some important characteristics of colon infections of the urinary tract, which we are about to discuss, were unknown to them, and asserted that even at the present time

[3] Brit. Med. Jour., 1904, ii, 1553.
[4] Osler's Modern Medicine, vol. iv, pp. 567–568.

this condition is frequently unrecognized. As early as 1887, Clado,[1] in his classic work, referred to finding a rod-like bacillus in the urine of patients suffering from urinary symptoms. In 1888 Albarran and Hallé[2] described "une bactérie pyogène" in certain urinary infections. Later, Krogius, of Helsingfors,[3] reported a motile, roddy bacillus in pathological specimens of urine, and was the first to conclude that this bacillus and those found by Clado and Albarran and Hallé were most probably identical with the Bacillus coli communis, which Escherish in 1885 found in the feces of babies. In 1893 Renault[4] published his comprehensive study, "Du bacterium Coli dans l'infection Urinaire," and only a year later Escherich made his first report to the medical society of Styria on 7 cases of cystitis in children caused by the Bacillus coli communis. This was followed in 1896 by the further report of 29 cases by his pupil, Trumpp.[5] These observations gave new impetus to the study of similar cases.

Although Escherich, Trumpp, Finkelstein, and others have cleared up the clinical picture of Bacillus coli cystitis and pyelitis, the diagnosis is still seldom made, either in infants or in adults. This is especially so in the case of the latter, because since this condition has been studied almost exclusively by pediatricians, we have obtained the impression that the disease is confined to children. As will be seen, however, a strikingly similar picture may also occur in adults.

Channels of Infection. There are four routes by which an infection of the urinary tract takes place: (1) The ascending, by way of the urethra (urogenic); (2) the descending, by way of the blood stream (hematogenic); (3) infection by contiguity, as from the rectum or any other portion of the large intestine, or directly transperitoneal; (4) through the lymphatic vessels.

Posner[6] and his pupils[7] proved experimentally the occurrence of hematogenic infection. Wrede's[8] experimental results in connection with the transperitoneal route are more doubtful. Beyond question the opinion of Escherich is correct, namely, that the infection in the vast majority of cases is ascending (urogenic). This fact also explains the prevalence of the condition in females; because the Bacillus coli, being a more or less constant inhabitant of the vulvovaginal ring, easily migrates under favorable conditions through the short female urethra into the bladder. Lenhartz found, out of 80 primary pyelitis cases, 74 in women.

The mere presence of the colon bacillus in the urine, without any further manifestations, does not mean an active infection. The Bacterium coli in some cases seems to thrive in the urinary

[1] Thèse de Paris, 1887.
[2] La Semaine Médicale, 1888, p. 303.
[3] Archives de médecine expér et d'anat. patholog., 1892, tome iv.
[4] Thèse de Paris, 1893.
[5] Münch. med. Woch., 1896, p. 1009.
[6] Berl. kl.in Woch., August, 1894.
[7] Ibid., September, 1900.
[8] Centralbl. f. Chir., xx, 577.

tract without damaging the immediate soil, giving rise to no symptoms, and producing only bacteriuria or bacilluria. Additional factors must come into play to enable the parasite to become offensively active. Nevertheless, I doubt if bacteriuria is ever entirely harmless. Probably there are transitional stages from "simple" bacteriuria to cystitis or cystopyelitis.

In this connection I believe that a chilled pelvis or abdomen, an obstructed and dilated ureter, a ren mobilis, stagnation of urine in pregnancy or post partum, and like predisposing factors are by no means essential to the production of a urinary infection. Frequently in hitherto healthy people the first sign of such a condition appears acutely, just as does pneumonia, typhoid fever, or any other acute infectious process. As in other infectious diseases, the fundamental cause of the form of pyelitis under discussion depends upon the powers of resistance of the human body at a given moment to the colon bacillus.

Symptomatology. The presence of the Bacterium coli in the urinary tract may cause general or local symptoms, or both. There may be an infection of the bladder or upper urinary tract without any noteworthy local symptoms, or these may be so slight as to be obscured by violent general symptoms, such as high fever, chills, general malaise, etc. Sometimes there is present only a slight evening fever, with paleness, anorexia, and general lassitude of apparently unknown origin, since nothing points to the urinary organs. This is the case in adults, while in babies a high or slight fever, continuous crying, and vomiting may mask the basic condition. Before such cases the physician stands confronted by insurmountable diagnostic obstacles. The lungs are examined time and again, the ears appear normal, there is nothing abnormal in the throat, nor is there the suspicion of any rash.

This difficulty in diagnosis was shown in one of my cases. Baby K., girl, aged nine months, healthy looking, breast-fed, for a few days showed general malaise and restlessness. Suddenly the temperature jumped to 104°; the baby appeared seriously sick, vomited, and refused the breast. A careful general examination did not reveal anything of importance. Although the intestinal tract was thoroughly emptied, the temperature remained 104° for the next two days, without any further clew as to its cause. While examining the baby, micturition set in, and to my surprise the urine gushed out like a white thread. Instantly the diagnosis was obvious. The microscopic and bacteriological examination of the urine confirmed the diagnosis of a colon infection of the urinary tract. The condition disappeared within the next week under appropriate treatment.

In children, especially girls, as well as in adults, this form of infection may go on for weeks or months after an undiagnosticated acute attack has subsided. Young girls in whom such a chronic infection exists may suffer from exacerbations of fever several

times a year, without any positive local signs. In some cases, older children at least, point to the seat of pain, complain of frequent, painful micturition (cystitis), or show some dysuric symptoms combined with pains in the back and right or left flank (pyelitis). It is just this irregular, ephemeral fever which puzzles the physician. Sometimes the temperature reaches 104°; remains several days at this height, and suddenly drops to subnormal. The child is afebril for days or weeks, only to suffer a new febrile paroxysm. Again the fever curve may closely simulate malaria and many times has been mistaken for it (Baginsky). Frequently, however, the fever resembles that which we see in septic or pyemic conditions.

Lenhartz,[9] in his important contribution to the study of pyelitis, tries to explain these febrile relapses. The relapses which had been mentioned by other authors he shows to be due to the transportation of the infection from one renal pelvis to the other—bilateral pyelitis. But he expressly states that the relapses can be brought about when the infection is limited to one pelvis by the inflammatory conditions temporarily subsiding only to appear again. This is the general rule. It is an interesting fact that some of the recurrent febrile attacks in pyelitis occur in connection with the menstrual period. A patient may be improving after the first attack of pyelitis, and may even have apparently completely recovered, but when the next menstrual period occurs it is accompanied by some slight discomfort, as lumbar pains and dysuric symptoms. The next menstruation aggravates the condition, and marked pain, vomiting, dysuria, and turbid urine appear, due clearly to a pyelitic relapse. Then treatment must be renewed. The same thing may repeat itself several times during the year, weakening the patient extremely. These relapses are to be found in postclimacteric women as well, only they do not occur at such regular intervals.

As if to complicate the picture of this enigmatic disease, it must be borne in mind that even severe cases of pyelitis may develop into and follow an afebrile course. The following of my cases illustrates this: Miss P., aged twenty-two years, always healthy. At the time she was expecting her menses she was caught in a drenching rain, rather lightly clothed. When seen on February 8, 1910, she complained of pain in the lower part of her left chest, radiating posteriorly to the left scapula. There was tenderness in the left flank. At no time was there any fever. On questioning, the patient recalled having had some slight burning sensation during micturition for the last few days. The urine, which was highly acid, showed pus cells, bacilli, and an enormous amount of almost exclusively spindle-shaped and caudate cells. This patient later suffered several severe relapses, mostly concomitant with her menstrual periods.

[9] Münch. med. Woch., 1907, No. xvi.

Pain, spontaneous or elicited by palpation, is an important symptom, and aids in arriving at the diagnosis, especially in older children and adults. The right or left flank is generally sensitive to pressure in pyelitis, while there is pain and tenderness in the suprapubic region in cystitis. This help, of course, is not to be had in babies. Even in children and adults the pain is sometimes confusing and is referred to remote places.

The following case will show how easily one may be misled in a diagnosis. Mrs. K., aged fifty-four years, always in perfect health, became suddenly ill with fever, vomiting, and anorexia. During the following few days she had vague abdominal pains, gagging, and gastric symptoms. A presumptive diagnosis of acute gastritis was made. The urine analysis, however, was as follows: High colored, turbid, strongly acid; albumin positive; microscopically, the field was full of pus corpuscles, motile bacteria of a uniform roddy type, and a few epithelial cells, but no blood corpuscles or casts. It became evident that a pyelitis existed. The course of the disease in this case was absolutely typical.

From November 23 to December 13, 1909, the patient was confined to bed. She had repeated attacks of vomiting; pains in the gastric region, fever, headache, and pain in the right flank. The urine was turbid, and contained pus and colon bacilli. This was the first pyelitic attack. During the second half of December, and January, February, and March she had apparently fully recovered. The patient gained in weight, did her regular housework, and considered herself in perfect health.

From March 24 to April 12, 1910, she was again seriously ill, with fever, pus in the urine, and a repetition of all the previous symptoms. After an apparent recovery, similar attacks recurred between May 19 and 25, and between August 13 and September. At each attack the urine, upon repeated examination, showed the presence of pus and bacilli. A radiographic examination excluded the presence of a stone in the kidney, which was highly improbable from the analysis of the clinical facts.

The great mutuality which exists between both kidneys should always be remembered. Indeed, the renorenal reflex is rather a source of error than a help.

To one especial feature I wish to briefly call attention. The sudden pain which may occur with an acute attack of pyelitis is mostly localized to the lumbar region. It is not of that lancinating, shooting down along the ureter type, found in so-called renal colic due to a stone in the pelvis of the kidneys. Even with concomitant vesical symptoms I have not seen true "colicky" pain in a pyelitis. The pain is dull, localized, that is to say, "renal" in character.

Urine. The main, basic point in this often puzzling disease is the urine. There is no other sign of equal importance to the urinary findings. The discrepancy between a negative physical examination and a serious general condition in a given patient

should make us think of cystopyelitis, just as we are accustomed to think of otitis, and "urine analysis should never be omitted in a case of obscure high or often repeated fever, even in infancy" (Holt).

The urine in cystopyelitis due to colon infection is strikingly characteristic. The points of importance are the highly acid reaction, at times a certain hue due to its color and transparency, and a definite cytological and bacteriological picture. To these Briscoe[10] adds that the specific gravity is rather high, higher than one would expect from the paleness of the urine.

As said before, the urine in this form of cystitis and pyelitis is always acid, highly so. The markedly acid reaction is characteristic of this disease. I have kept such specimen of urine for two weeks in open bottles at room temperature, and they still gave a distinctly acid reaction. This peculiar phenomenon has attracted the attention of scientists, but as yet a satisfactory explanation has not been given.

Pyelitic urines are said to be peculiarly pale, milky in their appearance. As a general statement this is wrong. The milky hue, this opalescence, is to be found in chronic cases, and then mostly during the intermissions. In acute cases, and in chronic cases during an acute exacerbation, the color rather deepens, the urine is concentrated, and the output diminished. The urine is simply cloudy, more so in cases of cystitis, less in pyelitis. In fact, in an acute febrile case a fresh specimen of urine that is cloudy and acid when examined at the patient's bedside means, with rare exceptions, only one thing—cystopyelitis.

The cause of the cloudiness is readily understood from a microscopic examination of the urinary sediment, which reveals pus cells, sometimes the entire microscopic field being full of them. They are mainly of the polymorphonuclear type, but some are mononuclear leukocytes. Besides, there are present epithelial cells of the squamous type, either aggregated in a shingle-like manner or solitary, caudate and spindle-shaped ones intermingled. Here and there a red corpuscle can be seen. Just as important as pus cells is the presence of rod-like, motile bacteria which, morphologically, as well as by subsequent bacteriological examination, are shown to be the *Bacillus coli communis*, sometimes present in pure culture. More rarely other microörganisms, such as the streptococci, staphylococci, Bacillus lactis aërogenes,[11] Bacillus bifidus Tissier,[12] are the cause of the inflammatory condition of the urinary tract. However, in the vast majority of cases of primary cystopyelitis with acid urine the Bacillus coli is the causal factor.

Casts in pure cases of pyelitis are not present, or can be seen

[10] The Lancet, 1909, ii, 1269.

[11] Escherich u. Pfaundler in Kolle-Wassermann's Handbuch d. path. Mikroorg., vol. ii.

[12] Centralbl. f. Bakt., 1909.

only occasionally, in acute and severe pyelitic inflammations. They soon disappear from the urine, and the pyelitis takes its ordinary course. Abt[13] is the only one to mention this rapid disappearance of casts. He also justly appreciates their pathological significance. Their temporary presence can only be explained on the grounds that the severe local inflammation of the renal pelvis involves the contiguous portions of the kidney proper, giving rise to conditions which vary from a simple "febrile" albuminuria to more severe parenchymatous and interstitial alterations of toxic and infectious origin.

If casts persist and other morphological kidney elements are present, together with corresponding clinical symptoms, the existence of a hematogenic invasion by the coli bacillus may be presumed, a true nephropyelitis, or a Bacillus coli septicemia may be the underlying cause of the infection, or an ascending infection may have definitely localized in the kidney.

Albumin is found in very purulent cases, and is proportional to the amount of pus present.

As has been said, during the acute stage of an uncontaminated case, a look into a hanging drop reveals, besides pus and epithelial cells derived from the urinary tract, uniform, roddy, motile microorganisms, which are colon bacilli (Escherich). Later, in the course of the disease, colon bacilli and epithelial cells decrease in amount, sometimes disappearing entirely for a time, and pus cells cover the field. Often the Bacillus coli communis prepares the ground for a secondary infection by staphylococci and streptococci. Many of the known purulent cases with various microörganisms present in the urine, but no colon bacilli, are to be explained in this way. I have seen cases of colon infection, which in time became ordinary purulent cases, which no one would suspect of having been originally of the pure colon type, unless they were traced throughout their entire course. Peculiarly, the urine always and invariably remained acid.

Chvostek and Egger[14] showed that care must be exercised in deciding upon the diagnostic and etiological value of microörganisms in the urine. These authors pointed out that during repeated febrile attacks in malaria and tuberculosis the urine was loaded with staphylococci, which had nothing to do with the basic disease. That the Bacillus coli communis is the real etiological factor of the symptom complex we have just analyzed was definitely proved serologically by Escherich and Pfaundler,[15] especially by the latter, who showed that the Bacterium coli from the urine in cases of colon pyelitis is agglutinated by the serum of the same patient. Although Kohler and Scheffler[16] found that such an agglutination may take place with normal serum, Jochmann[17] states that agglu-

[13] Jour. of the Amer. Med. Assoc., xlix.
[14] Wien. klin. Woch., 1896, No. 30.
[15] Kolle-Wassermann's Handbuch d. path. Microörganism.
[16] Münch. med. Woch., 1900, p. 787.
[17] Deutsch. Archiv f. klin. med., 1906, Band xxxvii.

tination with serum of higher dilutions (1 to 80 and over) points clearly to a colon infection.

Although it is often mentioned that the urine in cystopyelitis is, as a rule, cloudy, it would lead to errors to examine only cloudy urines. Sometimes a urine is perfectly clear, and we suspect nothing; but such a limpid urine may be deceptive. This was the case in W. R., a girl, aged about eleven years, who had had several febrile attacks. She would improve for a few days, only to again relapse, with chills and high fever. On account of backache and general malaise in the beginning, influenza was thought of; then typhoid fever came to the front. When I saw the child the physical examination gave an absolutely negative result. The urine was perfectly clear, albumin negative, but a microscopic examination revealed a few pus cells in every field, evidently the last traces of a subsiding pyelitis. Therefore, it should be emphasized that a microscopic examination is the only sure means of making a diagnosis.

Diagnosis and Differential Diagnosis. Cystopyelitis has been and continues to be confounded with many other febrile diseases.

The mild form, with its general malaise, backache, headache, and slight elevation of temperature, is usually mistaken for "influenza." One can only escape this error by systematically examining the urine.

In the grave acute cases a diagnosis is at first impossible. They begin with high fever, sometimes a chill (English authors report rigor as one of the first symptoms. I have not observed this, and am inclined to look upon it as a uremic manifestation), and more or less severe vomiting and gastric or abdominal pains usher in the attack. Appendicitis is thought of if the pain is referred anteriorly and downward on the right; pneumonia, if it radiates laterally or backward and upward; cholelithiasis or cholecystitis, if the pain is referred around the waist in a right-sided pyelitis; or if vomiting is severe and the epigastrium is painful, one may well think of gastritis. Rolleston has even described a "gastric type" of pyelitis. A careful study of the pain, however, will greatly help in locating the original source of infection.

The more protracted cases of pyelitis, with general indefinite symptoms, cephalalgia and fever, often resemble typhoid fever more than anything else. When we consider that the pulse in pyelitis is rather bradycardic, it is small wonder that many cases of pyelitis are regarded as typhoid. Attention has been called to this by Hartwig.[18] In cases of pyelitis with inconspicuous urinary manifestations even the Widal, as pointed out by Lommel,[19] may lead one astray. One should also think of a colon infection of the urinary tract superimposed upon typhoid with an atypical course

[18] Berl. klin. Woch., 1903.

[19] Münch. med. Woch., February, 1902.

(Neufeld[20]), a possibility readily explained, if the anatomicopathological changes of the intestines are kept in mind.

In young girls with general poor health, with or without exacerbations of fever recurring several times during the year, pyelitis is often mistaken for anemia, chlorosis, even latent tuberculosis, or for malaria, and is treated accordingly. In this respect the following case is especially suggestive:

Mrs. S. F., aged twenty-one years, married seven months. As a girl she was perfectly healthy. Never had any medical attention except for slight "sore throat" some years ago.

Present Illness. During the first week after her marriage frequent micturition set in, accompanied by a burning sensation. On account of this she often suppressed urination. She felt some fulness in the suprapubic region, and pain was elicited by pressing over that region. This condition lasted for about two months. She paid no attention to it, as she became spontaneously better. She felt comfortable until March, 1910, when the former trouble reappeared. On March 13, 1910, on awakening, she felt a sharp pain in the right side, which has kept up ever since. She had lost 21 pounds during seven months, was always tired, and became pale and thin. Her menstrual periods were regular after her marriage. On account of the pain in her side she saw a doctor on March 22, 1910, dreading possible "consumption." When seen by me at the office her tempretaure was 99.4°. There was a slight laryngeal cough, but her physical examination was otherwise negative, except for slight sensitiveness on pressure in the suprapubic region and right flank. Two diagnostic possibilities suggested themselves —either marital gonorrhea or latent tuberculosis. In making a vaginal inspection, the large, open-mouthed meatus urethræ externus impressed me, a fact which afterward was remarked independently by her regular physician. However, not a drop of blood could be expressed from it (gonorrhea ?). The subsequent microscopic analysis of the urine, which I give here from my records, was: "Masses of pus cells; quantities of rods; no erythrocytes; bladder epithelia and caudate cells present." The diagnosis of cystopyelitis was suggested (see microphotograph).

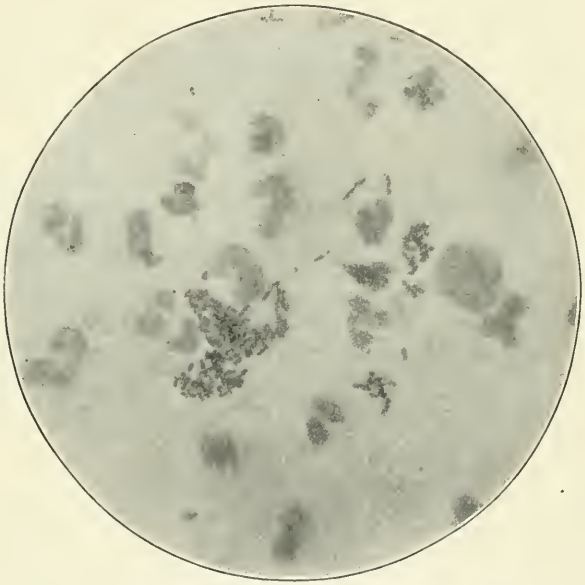
Under appropriate treatment the patient completely recovered, and gained in weight. Several urine examinations, the last in October, when the patient was in the eighth month of pregnancy, did not show a single pus corpuscle. I was informed by her physician that the patient had a normal parturition in November, 1910.

Often pyelitis is taken for a nephritis; at least, this is my experience. But after a week or two the patient apparently recovers from what was thought to have been serious kidney trouble. It is important to carefully analyze the urine in order to fix the diagnosis. As the albumin test is positive in every purulent pyelitis, only a thorough examination of the urinary sediment will be of value.

[20] Deutsch. med. Woch., No. 51, p. 825.

The lack of casts and renal epithelium, or their quick disappearance after the initial exacerbation, the presence of pus cells and of epithelial cells from the renal pelvis, all speak against the diagnosis of nephritis, however alarming the initial symptoms may be.

I wish to draw especial attention to two differential diagnostic points: (1) In some cases of pyelitis it is difficult to decide whether we have to deal with a primary pyelitis or with conditions secondary to a calculus. This should always be taken into consideration and a radiographic examination made by one thoroughly versed in such work. (2) The possibility of the presence of the tubercle bacillus



Photomicrograph of the urinary sediment from a case of colon bacillus cystopyelitis, showing pus cells and bacilli.

in the urinary tract, a true tuberculous infection, should always be borne in mind. Sometimes a mixed infection by both the tubercle and colon bacillus is the basis of the urinary manifestations.

Conclusions. 1. The disease which we have had under consideration is well defined, both etiologically and clinically, and strikingly resembles in this respect the so-called infectious diseases. The Bacillus coli communis is the most frequent organism causative to and characteristic of the disease.

2. Cystopyelitis is a febrile disease; the fever is often of the relapsing type, extending over variable periods of time.

3. Any obscure fever, as well as any unaccountable anemic condition in girls, with or without fever, is suspicious of latent pyelitis. Acid, turbid urine, containing pus cells and the Bacillus coli communis, is a positive finding confirmatory of such a condition.

REVIEWS

A Manual of Pathology and Morbid Anatomy. By T. Henry Green, M.D., F.R.C.P., Consulting Physician to the Charing-Cross Hospital, etc., London. Revised and enlarged by W. Cecil Bosanquet, M.A., M.D., F.R.C.P., Assistant Physician to the Charing-Cross Hospital, etc., London. Eleventh edition. Pp. 642; 250 illustrations. Philadelphia and New York: Lea & Febiger, 1911.

Much as it may be deplored by those who insist that knowledge must be acquired through reading "by and large," there can be no doubt but that the compendium occupies an important place in the libraries of both students and physicians. This may well be a matter of necessity in both instances, the student needing a ready and brief reference work to prepare for recitations or examinations, the practitioner being obliged, because of limitation of time, to refer to such a work for points that have become hazy or for a clear and concise statement of facts of recent development whose details are not already familiar to him.

The enormous and rapid advances made in modern pathology make necessary much enlargement of the older books and a corresponding condensation of the entire material presented, all of which must be done with clear perspective and thorough sense of proportion. Pathology is gradually coming into its own as a broad biological science; only as such can it advance; and the modern writer of works on pathology must not limit himself to pure morphology lest he be found lagging behind in the rapid march of progress and improvement. Thus he must have a clear conception not only of pathological physiology, pathological chemistry, bacteriology, immunology, pharmacology, indeed of all the subdivisions of medical and biological science which can in any way help in unfolding the mystery of disease and morbid processes. Bosanquet is well equipped to write on this dynamic side of pathology, and is admirably chosen to bring up to date in its eleventh edition Green's *Manual of Pathology*. He has elected to preserve much of the original form of the book presenting the subject in the usual two divisions, general and special pathology. The former division includes, with the usual subjects, a thorough and comprehensive discussion of both tumors and the various vegetable and animal parasites. At first glance the amount of space devoted to

the animal parasites might seem disproportionate, but a retrospect of the rapid increase in our information concerning these organisms awakens a realization of the necessity for their full consideration in this book.

In the same fashion the subject of immunology is given considerable space even to the point of including a résumé of the technique of the Wassermann test for syphilis. Whereas, general pathology occupies 408 pages, special pathology is limited to 200 pages. In this small space the reviser apparently has felt the need for a careful presentation of some of the more important and better-known subjects, with a very brief consideration or complete omission of some of the rarer and less completely studied conditions. Thus, the spleen and lymphatic apparatus are discussed in two pages, the presentation of the pathology of the skin is very limited, the adrenals and the thymus barely mentioned (and then only in the section on general pathology), and numerous rare and obscure conditions omitted entirely. On the other hand the liver, pancreas, and gastro-intestinal tract, the kidneys, and circulatory apparatus receive excellent discussion, the subject of nephritis being especially well treated.

The book is well illustrated, durably bound, printed in fairly large type on heavy, slightly glossed paper, and can safely be recommended to any who wish a concise and authentic account of a complex, extensive and rapidly advancing subject.

H. T. K.

An International System of Ophthalmic Practice. Edited by Walter L. Pyle, A.M., M.D., Philadelphia, Member of the American Ophthalmological Society. Pathology and Bacteriology by E. Treacher Collins, F.R.C.S., Surgeon to the Royal London Ophthalmic Hospital and Ophthalmic Surgeon to the Charing Cross Hospital, etc., and M. Stephen Mayou, F.R.C.S., Surgeon and Pathologist to the Central London Ophthalmic Hospital, etc. Pp. 558; 3 colored plates, and 237 illustrations. Philadelphia: P. Blakiston's Son & Co., 1911.

This book consists of seven chapters and an appendix. The descriptions are arranged with reference to pathological processes rather than to anatomical divisions. Such classification avoids repetition, inasmuch as the same process commonly involves more than one of the anatomical structures. The descriptions are, as a rule, brief, so that the work cannot be regarded as entirely elementary; being evidently intended for those already conversant with the general principles of pathology, as is indeed quite logical in a treatise upon the pathology of a highly specialized organ like the eye, to the study of which the student must come prepared by some previous knowledge of general pathology. At the same time

certain leading facts common to pathology in general are set forth; thus, inflammation is briefly described, the newer concepts with their terms, antigens, toxinogens, agglutinogens, precipitinogens, etc., are defined; Ehrlich's "side-chain theory" is given, etc.

The first chapter treats of aberrations in development; these are classified in accordance with the particular germinal membranes from which the different structures of the eye are developed. Each section opens with a very brief description of the normal embryonic development.

Neoplasms are considered in the second chapter. They are divided according as they arise from the cuticular, neural, or mesoblastic layers, metastatic growths, and cysts. Derangements of the fluids and vessels, injuries, inflammation, parasitic diseases, and degenerations occupy the remaining chapters. The appendix describes the practical methods of examining the different structures of the organ.

There are now two good treatises upon the pathology of the eye in the English language—this one and that of Parsons, so that the student need not necessarily be conversant with a foreign language, especially German, for information upon this subject. To say that the descriptions are very brief—*e. g.*, a few lines only are devoted to a consideration of the mode of transference of sympathetic ophthalmitis, which has been the subject of so many hypotheses and discussions—is not to bring adverse criticism, but only to indicate what a wide subject the pathology of the eye has become. The reader who desires a short account of the views held at present upon the different subjects of ocular pathology has in this work a source of information to which he can turn with confidence for answer to his inquiries. T. B. S.

Collected Papers by the Staff of St. Mary's Hospital, Mayo Clinic, Rochester, Minnesota, 1905–09. Pp. 668; 226 illustrations. Philadelphia and London: W. B. Saunders Company, 1911.

In a *Foreword* the authors state that they trust this volume "will be accepted for just what it purports to be, namely, an indexed collection of reprints." The editor is Mrs. M. H. Mellish, and the editing has been well done.

There are fourteen authors, and their work is represented by sixty-six papers, of varying length, importance, and interest, with the illustrations which have become so familiar a sight in recent years. Thirty papers deal with the alimentary tract, and eleven with the thyroid; while the remaining twenty-five papers are on such subjects as Hernia, surgery of the Genito-urinary Organs, Surgical Technique, etc.

It is impossible to review a work of this kind, and anything we could say would be quite useless. All these papers have been read when they appeared, and are familiar to surgeons everywhere. It is convenient to have them in handy form for reference; and it is pleasant to learn that the volume of reprints for the year 1910 is about to be issued from the same press; but it is almost paralyzing to see the amount of work being done, and to realize the immensity of its executive and administrative aspects.

It used to be a great thing if a surgeon could record so many "centuries" of cases; now, unless one has a few thousand operations from which to draw conclusions, he might as well keep his mouth shut for all the influence his opinion will have with the average "bounder" who storms the popular surgical clinic and "swears by" the surgeon with the most amazing figures. But we venture to think, and feel sure the brilliant chiefs of the surgical clinic of Rochester agree with us, that while dazzling statistics may bring notoriety to a surgeon, it is the power to think, to plan, to act, and to teach which brings him his true renown; that, when all is said and done, one man may know more from an experience of forty cases than another from four hundred or four thousand; that the man is greater than his work; that, when he is gone from his place, his absence will be felt not because another's hands are doing the work once done by his, but because his personality, his forceful character, his leadership is lost, and because these cannot, like the mantle of the prophet, fall on the shoulders of another.

A. P. C. A.

THE PRACTITIONER'S VISITING LIST FOR 1912. Pp. 192; 3 illustrations. Philadelphia and New York: Lea and Febiger.

AFTER twenty-eight years of continuous existence *The Practitioner's Visiting List* is too well known to the medical profession to require introduction. A more convenient, compact, and useful addition to the equipment of the practising physician than this little volume would be difficult to find.

The bulk of the book consists of pages of blanks so arranged that a daily record of patients seen as well as the patients' accounts may be quickly and easily kept. The adoption of such a system as this would go far toward lessening the not inconsiderable loss sustained by the majority of physicians as the result of careless bookkeeping. Additional pages are arranged for recording data relative to obstetric practice, births, deaths, vaccinations, and other important memoranda.

There is no practising physician who from time to time is not confronted with the urgent necessity for obtaining information on certain points. With this fact in mind, the text portion of *The*

Practitioner's Visiting List has been carefully compiled with a view to furnishing information, of the kind shown by long experience to be most often needed, in a concise and easily accessible form. Among some of the subjects covered in the thirty odd pages of text may be mentioned a scheme of dentition; tables of weights and measures, including admirable comparative scales by which ordinary weights and measures may be rapidly and easily converted into their exact equivalents in the metric system; the most important tests used in urine analysis; incompatibles; poisons and their antidotes; a table showing the differential points in the diagnosis of the commoner eruptive fevers; a remarkably complete table of doses based on the new United States Pharmacopœia; and finally directions for ligating the larger arteries.

The book, which is durably bound in flexible leather, is conveniently wallet-shaped, and is of a size that fits the pocket and may be easily carried.

To every practising physician who has never availed himself of this decidedly practical little book, *The Practitioner's Visiting List* may be heartily recommended. The many, however, who for years have facilitated their labors by its use, will welcome the announcement of the volume for 1912. G. M. P.

Diseases of the Stomach and Intestines. By Robert Coleman Kemp, M.D., Professor of Gastro-intestinal Diseases in the New York School of Clinical Medicine; Visiting Gastro-enterologist to the New York Red Cross Hospital; Gastrologist to the West Side German Dispensary; Consulting Physician, Gastro-intestinal Diseases, to Manhattan State Hospital. 280 illustrations. Philadelphia and London: W. B. Saunders Company, 1910.

Dr. Kemp has prepared a very careful and thorough text-book covering all the diseases of the stomach and intestines, but omitting those of the liver and pancreas. This omission is justified by precedent, although, to an increasing extent, these two organs are coming to be recognized as an essential part of the digestive system. On the other hand, he has boldly included typhoid fever and appendicitis, the former particularly never being assigned its proper place among diseases of the intestines in formal works on practice. Doubtless, if there were any reason for it in an American text-book, Dr. Kemp would have included cholera also.

Very little excepting praise can be said of this book. It is intended to supply, as far as a book may, clinical instruction for those physicians unable to take special courses in centres of medical education. That it is also an admirable adjunct to such clinical instruction is a matter of course.

It does not vary greatly in manner and matter from other text-books on this subject, but the information is well classified and the different tests are arranged so that reference to them is very easy. Not all the tests are given. For example, Sahli's fat test for the quantitative estimate of the gastric juice is omitted, and some of the later tests for gastric cancer, that have probably assumed importance only since the manuscript was sent to the printer, but the first has not been generally employed and the others have yet to demonstrate their usefulness.

The sections upon the physical examination of the abdomen in various diseases of the stomach are brief, and to the reviewer it seems that more detailed information under these paragraphs would have been advantageous. On the other hand, the symptomatology is usually fully given and the laboratory methods are also thoroughly discussed. The sections devoted to treatment are quite full. The illustrations are numerous and some of them appear unnecessary, but what to insert and what to omit is a matter of individual judgment. As an expression of personal opinion the reviewer regrets that photographs of the nude female should be used to display markings, indicating the position of organs, physical signs, etc. References to literature are few. In a text-book of this character they are probably not needed, but it seems as though it might have been useful to have called attention to the most important works in a brief appendix. The style is clear and the book making satisfactory. J. S.

PULMONARY TUBERCULOSIS AND ITS COMPLICATIONS. By SHERMAN G. BONNEY, A.M., M.D., Professor of Medicine, Denver and Gross College of Medicine, Denver, and Director of the National Association for the Study and Prevention of Tuberculosis. Second Edition; pp. 955; 243 Illustrations, including 31 in colors and 73 *x*-ray photographs. Philadelphia and New York: W. B. Saunders Company, 1910.

THE demand for a second edition of this work within two years after the publication of the first is very good evidence that such a work was really needed. The original book, and this applies equally well to the present volume, was designed especially for the use of general practitioners whose opportunities for clinical study may have been somewhat limited. It is therefore devoted essentially to the clinical aspects of tuberculosis, and emphasis is laid on practical considerations. While a thorough review has been made of all the important contributions in literature, only the essential and tried have been used. There is a remarkable absence of disputed theories and personal hobbies, and yet the reader is made acquainted with the author's viewpoint on practically every subject

and made to feel that this opinion is well supported by close study and careful observation extending over many years.

The book, while not purporting to be a guide for specialists, is nevertheless a thorough, systematic, and careful treatise on the subject of tuberculosis in its many and varied aspects. In the present edition five new chapters have been introduced, a few have been rewritten, and many materially amplified. There are 40 additional text illustrations, also 11 insert plates, 9 of which are colored.

Criticism might be made of the large number of illustrations and *x*-ray photographs, but these have all been chosen with considerable care and in almost every instance add much to the text. This is particularly true as regards the illustrations of shacks, tents, sanatoria, etc., from which the reader often derives many practical suggestions which the text could not give. The interspersion of a few well-chosen case histories also serves the same purpose and adds force and clearness to the argument. With Social Work playing so large a part in the handling of the problems of treatment and prevention of tuberculosis, it is gratifying to see this phase well discussed, and in close relation to this the several chapters devoted to Methods of Educating the Public and What the Public Should Know about Tuberculosis, are especially commendable. The reader is sometimes impressed with the preponderance of local coloring to some of the author's ideas, but this does not detract from the value of the book, and is probably unavoidable under the circumstances.

The book is well put up, on good paper, with clear, legible type, and an unusual dearth of typographical errors. The Index is very full and complete, and makes reference to any phase of the subject easy. The book has well fulfilled its errand, and should find a place in the library of anyone interested in the subject of tuberculosis. It should appeal especially to the general practitioner and the student of medicine, but it is not without considerable value to specialists or those working up the finer points of the disease.

F. H. K.

Progressive Medicine. A Quarterly Digest of Advances, Discoveries, and Improvements in the Medical and Surgical Sciences. Edited by Hobart Amory Hare, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College, Assisted by Leighton F. Appleman, M.D., Instructor of Therapeutics in the Jefferson Medical College, Philadelphia. Vol. III, pp. 328; 24 illustrations. Philadelphia and New York: Lea & Febiger, 1911.

The third volume of *Progressive Medicine* for the current year opens with a section on diseases of the thorax by William Ewart.

He first gives a most suggestive critical review of the discussion that has been in progress, especially in England, as to the exact scope and relative merits of the tuberculosis sanatorium, the dispensary, the tuberculin dispensary, and tuberculin treatment. He then takes up the use of continuous antiseptic inhalations and induced pneumothorax in the treatment of tuberculosis, recent advances in chest diagnosis, the pleura, the lungs, and their respective treatment, as well as the question of ventilation. The last half of Ewart's contribution is an admirable epitome of the latest teaching on many important points connected with physiological and clinical aspects of the cardiovascular system. The mechanism of both the normal and disturbed circulation is carefully considered; under the latter head auricular fibrillation and paroxysmal tachycardia are included. Edema and its cause, with especial reference to Fischer's colloidal theory of edema; Henderson's acapnial theory of shock; functional cardiac murmurs; heart failure, and heart treatment are some of the pertinent questions that merit especial attention.

Dermatology and syphilis are reviewed by William S. Gottheil. Among the large number of skin diseases discussed, he dwells particularly upon baldness and baldness cures, skin cancer, and the treatment of eczema. The major part of his article on syphilis is given over to a timely consideration of arsenobenzol. In view of the widespread attention that this remedy has attracted, Gottheil's thoughtful, critical, and wholly temperate summary of the present status of this drug is decidedly worthy of careful consideration. He has made no effort to review the enormous literature of this subject, but has devoted himself to a detailed analysis of a series of cases upon which he personally has employed the drug. The result of his painstaking observations forces him to conclude that, in spite of the extravagant claims so freely made for it, arsenobenzol, as a radical cure for syphilis, has proved entirely disappointing.

In an article of 126 pages, Edward P. Davis calls attention to the large amount of work that has been done in obstetrics. Under pregnancy he considers, at some length, pregnancy complicated by infection of the urinary tract with Bacillus coli communis, by gallstones, by cancer of the cervix, ovarian cysts, and fibroids; rupture of the uterus; eclampsia; and placenta prævia. Labor complicated by rigidity of the soft parts, sacral anesthesia during labor, labor obstructed by pelvic tumors, and the treatment of labor in contracted pelves may be mentioned as among the interesting topics included in his discussion of labor, while under the puerperium he pays particular attention to puerperal infection. After taking up obstetric surgery, particularly Cesarean section, he concludes with a consideration of the fetus and its appendages.

A final section of 45 pages embraces a highly instructive review of diseases of the nervous system by William G. Spiller. He points

out much that is of interest and importance in recent neurological work, at the same time emphasizing the subjects of brain tumor, tabes dorsalis, salvarsan in syphilis of the nervous system, and poliomyelitis.

Even a brief survey of the enormous amount of work that is today being done in medicine is sufficient to convince anyone that only through the medium of such a volume as *Progressive Medicine* can the physician, preoccupied with the exigencies of practice, hope to keep abreast of the rapid onward march of medical science.

G. M. P.

Hand-book of Diseases of the Eye. By Harry Caldwell Parker, M.D. Pp. 1303; 115 text engravings, a half-tone frontispiece, and 5 full-page chromolithographic plates with 26 figures. Philadelphia: F. A. Davis Co., 1911.

In presenting this volume, the author has desired to place before the student and busy practitioner, in a concise manner, the results of recent investigations and their practical application. The arrangement of the various chapters is necessarily similar to that found in other books of this character. He calls special attention to the chapter on the sclera which treats of the more recent investigations relating to the possible tuberculous origin of some of the forms of inflammation attacking this structure. He has also included a chapter on the bacteriology of the eye. In this chapter, under trachoma, he refers to the influenza-like bacillus described by Müller, but no mention is made of any relation that the Halberstädter and Prowazek "bodies" may have to this affection. Parker has done well in including in this work a short chapter on the relation of the eye and the nose, which will, I am sure, be of service to the readers of this volume. There has also been included a formulary containing a number of prescriptions serviceable in the treatment of ocular conditions. The text contains its full quota of errors, so prevalent in most first editions. A number of the sentences are not as clear and concise as they might be; for example, in speaking of the growths of the iris produced by tuberculosis and syphilis, it is stated that "both conditions are treated by the local treatment for the iritis, with which they are associated, and the constitutional cause of the inflammation." Further, in speaking of iridocyclitis, it is stated that "it frequently follows cataract extraction which has become infected." The reviewer realizes that there is probably nothing more difficult than the production of a satisfactory volume of this character, and he believes that after subsequent revisions this work will probably take its place with the number of excellent manuals or hand-books bearing on ocular affections that are already on the market. The press work is good, but the binding could be improved upon.

T. B. H.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Glucose in the Blood in Addison's Disease.—H. Schirokauer (*Berlin. klin. Woch.*, 1911, xlviii, 1505) has examined the blood in a case of Addison's disease with reference to its content in glucose. Determinations made on two occasions showed that the plasma contained 0.072 per cent. and 0.086 per cent. glucose respectively. These are normal values, though near the lower limits of the normal, and do not agree with the findings of Porges, who reported a hypoglycemia as one of the characteristic features of Addison's disease. Schirokauer, while admitting that a hypoglycemia may be met with, contends that it is not an essential part of the pathological physiology of adrenal insufficiency.

The Excretion of Creatin and Creatinin in Disease.—A. Skutetzky (*Deutsch. Archiv f. klin. Med.*, 1911, ciii, 423) has made a rather extensive study of creatin and creatinin excretion in disease. His material comprised 29 cases, chiefly diseases of the central nervous system, in which the excretion of creatin and creatinin have not been studied previously. The patients were placed on creatin- and creatinin-free diet to eliminate the exogenous source. The study included cases of epidemic and suppurative cerebrospinal meningitis, hemiplegia, syringomyelia, tabes dorsalis, transverse myelitis, epilepsy, dementia præcox, and also croupous and influenzal pneumonia, pleurisy, endocarditis, interstitial hepatitis, acute articular rheumatism, Basedow's disease, marasmus, diabetes mellitus and insipidus, and Banti's disease. The results are best expressed in Skutetzky's summary. (*a*) Creatinin: (1) Fever, associated with whatever patho-

logical process causes an increased elimination from the heightened protein metabolism. This is proportional to the height of the fever. After the fever has lasted for some time, or following a relapse, the amount diminishes. (2) In afebrile diseases of the central nervous system, in which neither the muscular tone is increased nor muscular exercise indulged in, the patients being confined quietly in bed (hemiplegia, myelitis, tabes, syringomyelia), the excretion is normal or subnormal. In those diseases characterized by excessive muscular activity (epilepsy), on the other hand, the creatinin is very greatly increased. In nervous diseases following the administration of salvarsan, an increased excretion appears on the second to the fourth day after the injection, lasting a few days. (3) The excretion is greatly diminished in hepatic disease where the function of the liver is disturbed; also in (4) diabetes mellitus and in Basedow's disease. (5) In marasmus the values are subnormal; in diabetes insipidus, practically normal. (6) A meat diet after a long period of milk diet causes a temporary increase. (*b*) Creatin: (1) In fever creatin is found constantly in considerable quantity. After the fever has lasted for some time, creatin may disappear. (2) In afebrile nervous diseases with the patients at rest, creatin is found in the urine only in traces. After muscular exercise (epileptic attack) the amount is large. Following salvarsan, an increased creatin excretion may precede the increase in the creatinin. (3) Creatin is excreted in considerable amounts in hepatic disease and in Basedow's disease.

Artificial Immunity Against Trypanosomes.—E. Teichmann and H. Braun (*Berlin. klin. Woch.*, 1911, xlviii, 1562) have been able to prepare a trypanosome vaccine from the dead organisms which may be preserved and the dosage of which may be accurately measured. By means of it they can produce an active immunity in mice. The animals exhibit no morbid symptoms from the vaccination and are protected from a fatal dose of living trypanosomes. Using the same vaccine, the authors have prepared an immune serum of high potency from rabbits. A single small injection of the immune serum protects mice against a fatal dose of the organisms, whereas controls which received normal rabbit serum always died.

Chemotherapy of Pneumococcus Infections.—J. Morgenroth and R. Levy (*Berlin. klin. Woch.*, 1911, xlviii, 1560) point to certain biological characteristics peculiar to the pneumococcus, on the one hand, and to trypanosomes and spirilla on the other. Thus, all are dissolved by bile salts, though the other pathogenic cocci are unaffected. In studying the effect of various derivatives of quinine on trypanosomes, Morgenroth and Halberstaedter found a body which exhibited a markedly destructive action against these parasites. Morgenroth and Levy have undertaken the study of the action of these same compounds in experimental pneumococcus infections in white mice. Several of the derivatives proved to be practically inert, but in "Ethylhydrocupreinsulfat" a substance has been discovered which has a definitely curative action in white mice in a certain proportion of the cases. The animals which recover are possessed of an active immunity to the pneumococcus. Other compounds are being pre-

pared and will be tried in pneumococcus and other bacterial infections, in an attempt to secure still better results. In the findings which they report at the present time, Morgenroth and Levy see the possibility of a successful chemotherapy of bacterial diseases.

A Modification of the Spectroscopic Test for Occult Blood.—K. Csépai (*Deutsch. Archiv f. klin. Med.*, 1911, ciii, 459) has modified the method of spectroscopic examination for occult blood so that the test may be rapidly and simply performed; its delicacy almost equals that of the color tests (guaiac, benzidin), and the results are not equivocal. Method: To 5 grams feces add 5 c.c. of glacial acetic acid, 5 c.c. of ether, and 5 c.c. of alcohol. Rub the mixture well in a mortar for two or three minutes, then filter through a dry, folded filter. To the extract add 1 to 2 c.c. of pyridin and then 1 to 3 drops of ammonium sulphide. In the presence of blood the spectrum of hemochromogen is now demonstrable. The following precautions are necessary in applying the test: (1) The patient must abstain from meat and green vegetables for three days preceding the test, since hemoglobin and chlorophyl will give it. (2) The ammonium sulphide must be kept in a dark bottle with glass stopper. Preserved in this way, it retains its reducing action for about ten days. (3) More than three drops of ammonium sulphide should not be used, since an excess diminishes the intensity of the spectrum. (4) The examination must be made immediately after adding the ammonium sulphide, since the spectrum soon fades. The test will detect blood in a dilution of 0.1 per cent. in the feces. This is not so delicate as the guaiac test, but much more reliable, since only blood will give a positive test if condition (1) is fulfilled.

A Contribution to the Chemistry of Blood Regeneration.—E. Masing (*Archiv f. exp. Path. u. Pharmakol.*, 1911, lxvi, 71) has attempted to discover chemical changes in the blood during active regeneration which might be correlated with the morphological and biological alterations known to exist. His preliminary experiments showed that the serum in experimental toxic anemias was richer in phosphorus than normal serum. Since phosphorus is an important constituent of cell nuclei, and, further, since nuclei are constantly being formed in large number during regeneration, Masing directed his attention to the various phosphorus compounds in the present study. Rabbits and geese were used as experimental animals. Comparative determinations of the phosphorus in normal and anemic animals were made. Total phosphorus, lipoid phosphorus, and nuclein phosphorus were quantitated in the serum and the red cells of the rabbit and in the red cells of the goose. In the serum of the anemic rabbits the phosphorus which may be extracted with alcohol-ether is increased above the normal. The erythrocytes of the rabbit are also richer in ether-soluble phosphorus. Masing finds also that the red cells of anemic rabbits contain considerable nucleinic acid, whereas normally it is present only in very small amounts. Similarly the nucleinic acid content of anemic goose blood is markedly increased. Masing concludes that the increased quantity of nucleinic acid and of phosphatids is to be interpreted as evidence of large numbers of young blood cells in the peripheral blood.

Entameba Tetragena in Manila and Saigon.—E. R. Whitmore (*Archiv f. Protistenkunde*, 1911, xxiii, 71) reports the study of amebæ from patients in Manila and Saigon. His material included stools from fourteen patients suffering with dysentery and the pus from an amebic liver abscess. The examination of this material revealed the rather surprising fact that only two species of amebæ were present, namely, Entameba tetragena and the non-pathogenic Entameba coli. Not a single example of Entameba histolytica was seen. It is evident, therefore, that in Manila and Saigon, Entameba tetragena assumes added importance as a cause of dysentery. Indeed, Whitmore believes that for these localities this is the usual causative factor in amebic dysentery, while Entameba histolytica is rather exceptional. Cultures taken from water showed only free-living amebæ, quite distinct from the parasitic varieties.

SURGERY

UNDER THE CHARGE OF

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The Employment of Novo-iodine in Surgical Tuberculosis.—Drachter (*Zentralbl. f. Chir.*, 1911, xxxviii, 1145) says that of the many substitutes for iodoform, as aristol, etc., none has seriously contended with it. The chief objections to iodoform are its offensive odor and toxicity. It often produces irritation of the skin and mucous membrane, which is not always limited to the site of application, but is found in other parts of the body also. Drachter has been trying out novo-iodine. Its chemical name is hexamethylenen, and its formula is, $C_6H_{12}N_4I_2$. It is mixed with equal parts of talcum. When it comes in contact with organic tissues, it is split up into iodine and formaldehyde. According to Schattenfroh, novo-iodine in the blood serum, pus, and physiological saline solution, in the strength of 1 to 1000, possesses a strong antibactericidal power, considerably stronger than that of iodoform or any of its substitutes. Drachter has employed it mostly in tuberculous diseases of the bones and joints, tuberculous caries of the ribs and sternum, spina ventosa, caries of the foot and hand bones, of the skull, vertebræ, and pelvis. He has also used it extensively in tuberculous affections of the soft tissues, especially in fistulæ and abscesses, as from the hip-, knee-, elbow-, and foot-joints. In open tuberculous conditions with suppuration it reduces the secre-

tion markedly, and favors the formation of red, fresh, and sound granulations. Large tuberculous cavities were filled with the novo-iodine suspension, so that it found its way into all angles; or they were packed with novo-iodine gauze or with ordinary aseptic gauze soaked in the novo-iodine suspension. A reduction of the discharges was observed to follow almost without exception. An especial advantage is that it is entirely without odor and, in addition, is markedly deodorizing, which effect is to be attributed to the formaldehyde which it contains. It has been employed as a deodorant with good effect in gangrenous appendicitis. It is completely non-irritating and non-toxic, and for this reason can be applied to the tender skin of a very young child. In animal experiments on rabbits, doses of 1 gram per animal kilogram were borne without difficulty. Its application caused no noteworthy pain. It was not applied to mucous membranes.

The Use of a Tubular Speculum in Peritonitis.—Kuhn (*Zentralbl. f. Chir.*, 1911, xxxviii, 1177) says that he has been employing for years short and long specula, like those used in the vagina and rectum, in the treatment of suppurative peritonitis. When a diffused inflammation is suspected, and a fluid exudate is supposed to be present, he makes a small incision in the abdominal wall, large enough to admit the speculum, and over some region still free from the inflammation. The speculum, provided with an obturator, is carefully introduced through the abdominal wound, which is then closed around it. It is then pressed inward slowly and carefully. Soon he removes the obturator, wipes out the tube with a pad on a long handle, and thus finds the way for deeper pushing of the obturator and speculum. By means of a good light he obtains a good inspection in the depth of the abdominal cavity, as in the pelvis or behind the stomach. The condition of the coils of the intestine can be determined, the state of their walls, and the presence or absence of adhesions or exudate. When he suspects that the exudate is circumscribed, by approaching it from the undisturbed side, he tries not to break into it, but is anxious to preserve it intact. The information thus obtained, and its relation to the prognosis and treatment are important. By this method all angles and pockets and spaces between the intestinal coils can be examined, especially in the deep parts, as the hypochondrium and pelvis. For every new introduction of the speculum, when that already in cannot be passed further, a clean one may be substituted. When, however, he comes on an exudate, Kuhn changes the position of the speculum to all parts that he can reach. When he irrigates, he prefers to make a second or third incision, with a speculum in each; although by passing an irrigation tube into a wide speculum, a single opening may be sufficient to carry on the irrigation. When the toilet of the deep parts is completed, a rubber or glass drainage tube is passed through the speculum to the desired part and is left there, the speculum being withdrawn over it. In ten minutes the abdominal cavity can be examined in all directions and provided with drains. In order that the omentum may not slip into the opening of the drainage tube, Kuhn often covers it with gauze to protect it from such an accident. He has treated his cases of peritonitis for years in this way. If he suspects the presence of a necrotic appendix, by working from the

less toward the most infected region, this can be removed. If a perforation or suppuration is encountered, the usual methods are adopted to contend with it.

The Technique of Operative Closure of the Intestine.—Voeckler (*Zentralbl. f. Chir.*, 1911, xxxviii, 1179) has been employing for some time the following method of closing the intestine opened by operation, as the duodenum after resection of the pylorus, and after all resections of the intestine, when a side to side anastomosis is to be made. The intestine is first freed from its attachment to the mesentery, and a purse-string suture of catgut, including the serous and muscular coats, is introduced in the circumference of the intestine near the place where it is to be divided. About 1.5 cm. from this suture, somewhat farther in the large intestine, the gut is divided between the blades of an intestinal clamp. A strong silk ligature is employed to close the open end of the intestine beyond where the purse-string suture is placed. This is tied with a slip knot so arranged that when the now closed end is inverted and the purse-string suture tied, by holding the end of the intestine with the finger and thumb of one hand and making a tug on the silk ligature it will unloosen at the slip knot and come out. As this is being done the purse string is being held ready to be tied as soon as the silk ligature is removed. After double knotting, the purse-string suture is cut short, and may then be covered over by a Lembert suture. The advantages of this method are as follows: No closed space is left at the end of the intestine between the two ligatures in which infected material can accumulate. The same danger arises when the enterotribe is employed. No foreign body is left in, as from the ligature or the crushed portion of the intestinal wall from the use of the enterotribe, which becomes necrotic. The method is simple, is carried out quickly and without special instruments. Voeckler observed no signs of hemorrhage from the untreated, divided mucous membrane.

Local Anesthesia in Operations on the Trigeminus Region.—Braun (*Deut. Zschr. f. Chir.*, 1911, ci, 321) says that the addition of adrenalin to cocaine solutions permits us now to operate under local anesthesia from injection of the larger nerve trunks in parts of the body where a tourniquet cannot be applied. The substitution of novocain for cocaine, permits us to inject a much larger quantity of the anesthetic fluid in the neighborhood of the nerve trunks without danger. Braun believes that in no place in the body will local anesthesia produce so great an advance as in operations on the trigeminus region. The technique for reaching the various branches is fully discussed. The advantages of local anesthesia in these operations are as follows: Resection of the upper jaw loses almost all its horrors and dangers, and becomes an entirely different operation from that under general anesthesia. No preliminary operation is necessary, neither a tracheotomy nor a ligation of the common carotid. Nor is the Kuhn tubage necessary, since little or no hemorrhage occurs. As the surgeon is not obstructed by the anesthetist, he can work unhindered to the end of the operation. After the operation the patient is as fresh as before, and is absolutely not collapsed. For tongue operations and

excision of the lower jaw the advantages are the same. Braun has done these operations for two years under local anesthesia without exception. The anesthesia and freedom from blood of the operative field were always complete, narcosis never being necessary. No patients died as the result of the operation. Of 8 cases of resection of the upper jaw, and of 12 operated on for cancer of the oral cavity, 2 had postoperative complications, a very small percentage. For injections into the orbit and the pterygopalatine fossa, no special dangers are associated, and there is no need of fear of wounding the vessels.

A Contribution to the Pathology of Renal Calculi.—Rosenbach (*Deut. Zschr. f. Chir.*, 1911, ci, 556) made a study of this question based upon experimental work on dogs. Renal calculi, as Ebstein and many others have shown, are formed by the collection together, of organic and inorganic material. For the formation of stones which give clinical symptoms, the *sine qua non* is a condition in which there is an increase of salts in the blood, a "diathesis." In this respect authors are agreed. On the other hand, it is known that this alone is not sufficient for stone formation. Clinical experience shows that in gout ("uric acid diathesis") the oxaluria, phosphaturia, and cystinuria, in most cases do not lead to the formation of calculi. In Rosenbach's opinion, the second factor in the formation of stone is to be sought not in the kidney itself, but in the blood. According to this suggestion, renal calculus is not a surgical condition. We may hope that the dissolvent work of the kidney may be aided by the ingestion of sufficient water. It would be the ideal method if, after the removal of the diathesis, the kidney could deal with the calculus alone. But severe and irreparable changes in the kidney may have been caused by the stone, so that surgical as well as internal therapy will be justified. The damage to the parenchyma will not be much increased by the operation, while by the removal of the obstruction an existing infection is permitted to heal.

A New Method of Operating for the Gastric Crises of Tabes.—Exner (*Deut. Zschr. f. Chir.*, 1911, ci, 576) operated on one case by Förster's method of dividing within the spinal canal the sensory roots of the tenth, eleventh, and twelfth dorsal spinal nerves. For four weeks after the operation the patient was free of trouble. Then the vomiting returned, but without the girdle sensation and without the pain accompanying the gastric crises. After a study of the question, Exner concluded that the vomiting is the result of the gastric movements which are controlled by the vagi, and that in some cases at least the primary cause is an involvement by the disease of the vagus or its centre, and that the pain is secondary to the vomiting. It has been shown by animal experimentation that not only is the vagus the motor nerve of the stomach, but that its division leads to pathological changes in its walls, as ulcers. Exner decided to divide the vagi at the cardia, before they gave off their branches to the stomach, and, in order to prevent the gastric complications, provide a gastrostomy through which a perforated drainage tube could be made to pass the pylorus into the duodenum. This was done to overcome the pyloric spasm that results reflexly from excess of acid con-

tents in the atonic stomach. The operation was performed on two cases. On the fourteenth day after operation the first patient began to take semisolid food by the stomach, and had no trouble from it. Eight days later the drainage tube was withdrawn until it reached only into the stomach. It was removed completely three weeks after the operation, and the fistula quickly healed afterward. While the patient before the operation was taking at least 0.3 grain of morphine daily, in the first week after operation she took only 0.03 grain, and from that time on did not take any morphine or any other drug having a similar effect. The second patient died three weeks after operation. The postmortem showed that there was a high grade of marasmus of all the organs and a well-encapsulated subphrenic abscess above the left lobe of the liver. No organic changes were observed in the stomach.

The Merits of Suprapubic Prostatectomy.—Squier (*Surg., Gynec., and Obstet.*, 1911, xiii, 254), after a consideration of the anatomical points, proceeds to the description of the suprapubic operation. The bladder should be opened by an incision large enough to admit two or three fingers, high up on the fundus of the bladder and close to the peritoneal attachment. This favors earlier closure of the urinary sinus than if the bladder opening is made low, which favors constant escape of urine. Squier does not enucleate the prostate *en masse*, as does Freyer, but each lateral lobe separately. The finger is inserted into the internal meatus and is made to break through the roof of the urethra. Access is at once given to the proper line of cleavage between the lobes, since at this point they lie in close apposition, being separated only by the capsule. The enucleation is begun by pushing the finger upward and forward, freeing the apex of the prostate from its attachment to the urethra and the triangular ligament. It is swept around the surface, and the lobe is hooked back into the bladder with its apex looking upward. Then a little separation of the mass from the bladder mucous membrane completes its removal. A similar procedure on the other side finishes the removal. The moment the prostate has been delivered the anesthesia is stopped. A drainage tube is inserted at the upper angle of the bladder wall and the lower angle is sutured tight to the tube. The abdominal wound is closed by a few figure-of-eight silkworm-gut sutures, one loop approximating the fascia and the other loop the skin. The operation done in this way can be accomplished in four or five minutes in most cases, and the patient need be subjected to complete anesthesia for but two or three minutes. A prostate without median outgrowth may be enucleated with practically no danger to the floor of the prostatic urethra and, therefore, to the ejaculatory ducts. If there is a median outgrowth the floor of the urethra posterior to the colliculis is removed, but this is of no great moment. By the suprapubic method all operative work is carried out behind the triangular ligament, and thus the preservation of the external sphincter prevents urinary incontinence. The keynote of the situation is that the patient should be trained for the risks of the operation, by preliminary nursing and preparation of the kidneys. If he succumbs, it is usually from renal insufficiency or from shock, and predisposition to this is increased by the length of time the patient is under the anesthetic. The indication is for the minimum of anesthesia.

THERAPEUTICS

UNDER THE CHARGE OF

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The Treatment of Gout.—Schmidt (*Münch. med. Woch.*, 1911, lviii, 1764) believes that gout is favorably influenced by continuous large doses of hydrochloric acid together with iodglidin. The hydrochloric acid treatment has been highly recommended by Falkenstein, and Schmidt confirms his results. He believes that this therapy is based upon a lowered metabolism due to a low gastric acidity or a lack of acidity, that may be demonstrated by test meals before the treatment is given. Schmidt says that acute attacks may be prevented by this treatment and that a strict diet is not essential. He advocates great care in the diagnosis of atypical cases of gout. The presence of urates may be demonstrated by the *x*-rays, and the uric acid content of the blood should be determined, together with the determination of the excretion of the exogenous and the endogenous uric acid. He describes simple tests which he believes are reliable.

The Treatment of Acute Attacks of Gout.—Falkenstein (*Münch. med. Woch.*, 1911, lviii, 1397) advises the use of injections of local anesthetics in the neighborhood of affected joints in acute gout. These local injections render the acutely inflamed joints almost painless and contribute much to the comfort of the patient. He uses for this purpose eusemin, giving one ampoule for mild cases, and two or three for the severer cases. Falkenstein discovered the beneficial effects of local anesthesia accidentally in the preparation of an acutely inflamed, gouty joint for exploratory puncture. The relief to pain was so great in this case that he has since made a practice of giving the injections for their therapeutic effect.

The Significance of the Wassermann Reaction in the Treatment of Syphilis.—Citron (*Therap. Monatsheft.*, 1911, xxv, 421) considers that the Wassermann reaction should be the guide in the treatment of syphilis. The test should be made with the original technique. A positive reaction indicates active syphilis; a negative reaction indicates either a latent or a cured case, and a doubtful reaction points more to latent disease rather than to a cured case. The Wassermann reaction should be repeated at intervals and a positive reaction always necessitates active treataent. The success of treatment is indicated by a change from a positive to a negative reaction. When treatment is instituted early after the infection this effect is obtained in a shorter time than when the treatment is delayed. Citron says that salvarsan often cures other manifestations of syphilis, but does not always result in a negative Wassermann reaction. He believes that some form of mercury should still be the main reliance for the treatment

of syphilis, but that it may often be combined with salvarsan with good effects. The Wassermann reaction is an important factor in the treatment of those patients with either indefinite luetic symptoms or no symptoms at all. It is also the only absolute indication to determine the length of time of the treatment in individual cases. Citron insists that the treatment should be continued until there is a persistent negative reaction. He believes that the Wassermann test is also of value to indicate the therapeutic effect of various antisyphilitic remedies.

The Treatment of Hay Fever by Hypodermic Inoculations of Pollen Vaccine.—Freeman (*The Lancet*, 1911, clxxxi, 814) reports 20 cases of hay fever treated by inoculations of pollen vaccine, with very beneficial effects in 16 cases. The best results were obtained with the use of the vaccine derived from the pollen of timothy grass. Freeman says that it is well known that individual patients are very susceptible to the pollen of certain definite plants, and the question naturally arises whether one kind of pollen vaccine may be more active in one case and another in another case. Although this point cannot be regarded as settled, it apparently is not so. He found that the pollen of Alopecurus pratensis gave good results, but only possessed one-quarter the strength of Phleum pratense (timothy grass). This ratio between the strength of a phleum extract and an alopecurus extract remained constant with different patients. Consequently, Freeman does not believe that it is necessary to select different types of pollen for the treatment of different patients. In considering the cases treated, Freeman says that there seems little doubt that there has been a distinct amelioration of symptoms. This improvement took several forms—a greater freedom from attack, the attack not so severe as in former years, and the attack sooner over, the constitutional disturbance not so great, and less asthma. The original article should be consulted for details of the dosage and the application of the treatment.

The Action of Atophan on the Purin Metabolism.—Starkenstein (*Arch. f. Exper. Path. und Pharm.*, 1911, lxv, 177) relates his experiments on the action of atophan upon the purin metabolism of various animals. He also tested its action in his own case. His experiments showed that the increased excretion of uric acid in dogs was coincident with a diminished output of allantoin, and that these two factors balanced one another. He explains this by a fault in oxidation of the uric acid to allantoin that normally occurs in dogs. Atophan caused a diminution of the uric acid excretion in hens which he attributes to a defective synthesis from urea. The experiments upon himself resulted in an increased output of uric acid that was transient and was followed by a period of diminished excretion. Starkenstein suggests the hypothesis that atophan hastens the breaking down of the nucleoproteids that are predestined to be the source of the endogenous uric acid. This increases the output of endogenous uric acid temporarily, and following this there is a diminished output of uric acid. This effect of atophan in hastening the excretion of the endogenous uric acid tends to prevent the deposition of uric acid in joints and cartilages. The good results obtained by different observers in the treatment of

gout may be explained in this way, although more evidence is necessary, both experimental and clinical, to support this view. Starkenstein does not believe in the theory that atophan increases the permeability of the renal epithelium to uric acid by a direct stimulating action upon the renal cells. The hypothesis of Starkenstein is not based upon sufficient experimental evidence, but if true, atophan will be a distinct addition to the therapy of gout.

The Treatment of Gonorrheal Arthritis with Injections of Tincture of Iodine.—Hildebrand (*Berlin. klin. Woch.*, 1911, xlviii, 1410) has used 5 per cent. tincture of iodine injected directly into the affected joints, and speaks very favorably of this method of treatment. During the first few days after the injection a considerable increase of the swelling of the joint occurs. This increase, however, subsides rapidly after a few days. Pain in the affected joint diminishes and the joint soon becomes more movable. Hildebrand says that there is no danger of adhesions forming as a result of the injections, and cites a case where the condition of the joint was absolutely normal as seen at autopsy six months after a series of iodine injections. Hildebrand warns against giving the iodine in too large amounts or in too concentrated a form, although he does not specify any definite amount.

The Activity of the Pancreatic Function Under the Influence of Copious and Moderate Water Drinking with Meals.—Hawk (*Arch. Int. Med.*, 1911, viii, 382) studied the problem of the influence of water drinking at meal times on the activity of the pancreatic function. The amylolytic activity of the feces, denoting, according to Wohlgemuth, the content of pancreatic amylase present in the feces, was taken as the index of the activity of the pancreatic function. The amylolytic values for the stools increased markedly during the periods of moderate and copious water drinking as compared to the control periods. Hawk draws the general conclusion that the ingestion of quantities of water at meal time, ranging in volume from $\frac{1}{2}$ to $1\frac{1}{3}$ liters, stimulates the pancreatic function in two ways: (1) A direct stimulation of the nervous mechanism of the pancreas brought about while the water is still in the stomach; and (2) an indirect stimulation brought about on the entrance of the increased volume of acid chyme into the duodenum. The drinking of water with meals ought, therefore, to bring about a more rapid and complete digestion and absorption of the fat and carbohydrate constituents of the diet, two observations verified by experimentation in the laboratory.

The Treatment of Sea Sickness.—Citron (*Berlin. klin. Woch.*, 1911, xlviii, 1646) says that veronal is superior to any other drug that has thus far been advocated for the treatment of sea sickness. The fact that it is often impossible to administer any drug by mouth for this affection led him to try the more soluble sodium veronal by rectum. He administered tablets of sodium veronal by the rectum, and says that a marked improvement in the symptoms occurred within one hour after its administration in this way. He also suggests that it may be given by rectum in the form of suppositories. It is probable that equally good results will be obtained with this remedy in car sickness.

The Immediate Effect on the Complement Fixation Test for Lues of Treatment with Salvarsan.—Craig (*Arch. Int. Med.*, 1911, viii, 395) gives tabulated reports of 250 Wassermann tests in cases of syphilis of all stages before and after treatment with salvarsan. From the analyses of complement fixation tests after the administration of salvarsan, Craig believes that the following conclusions may be safely drawn. The best results, as regards the disappearance of the complement fixation test and the occurrences of relapses, are obtained in the treatment of patients in the primary stage of lues, and the poorest in the treatment of those in the tertiary stage. Thus, 25 out of 31 in the primary stage, or 80.6 per cent., gave a negative reaction after treatment, while only 12 out of 22 in the tertiary stage, or 54.9 per cent., resulted negatively. The results in the secondary stage were also good as measured by the Wassermann test, since this test became negative in 100 of 135 second stage cases, a percentage of 74. Craig says that the complement fixation test disappears more rapidly after treatment with salvarsan in the tertiary stage of lues than in either the primary or secondary stage of the disease. However, he is only comparing the negative reactions of the 12 tertiary cases with the 125 of combined primary and secondary cases. The reaction in Craig's experience has disappeared during the second, third, and fourth weeks after treatment in the vast majority of the negative cases. The prognosis, both as regards the disappearance of the reaction and the occurrence of relapses, is dependent upon the strength of the reaction. It is most favorable in patients with a plus-minus reaction, and least so in those giving a double plus reaction. As regards the method of administration of salvarsan, the best results have been obtained in his experience from the intramuscular injection of the alkaline solution, and the poorest from the use of the neutral suspension. In justice to the intravenous method, however, it should be stated that a smaller number of cases have been tested, and it may be that this method will prove as efficient as the intramuscular. The complement fixation test reaction disappears more rapidly after the intravenous administration of salvarsan than after the intramuscular administration. As regards the disappearance of the complement fixation reaction, better results were obtained in patients who had previously received mercurial treatment than in those who had not, but the time of disappearance of the reaction was little affected. The great superiority of salvarsan over mercury as a specific remedy was shown in the rapid and apparently permanent disappearance of the reaction, after one or two injections of the drug, in patients previously treated for one, two, or three years with mercurials, and in whom the reaction had remained. The complement fixation test is of the very greatest value as a guide to treatment with salvarsan, and it is the only method we possess of determining whether lues is actually cured by any therapeutic agent. Finally, Craig believes that the data recorded in this paper eloquently sustained Ehrlich's modest claim that the introduction of salvarsan marks a considerable advance in the therapy of syphilis, an advance which is not due to accident, but to the result of systematic experimental work.

PEDIATRICS

UNDER THE CHARGE OF

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Mediastinal Causes of Chronic Cough in Children.—HERBERT FRENCH (*Brit. Med. Jour.*, 1911, clxxxi, 757) calls attention to the many cases of chronic cough in children which are not relieved by medication, and which show no obvious physical signs. These cases are often attributed to adenoids and enlarged tonsils, but a large number of them are due to enlarged glands at the bifurcation of the trachea. This enlargement is usually chronic and often tuberculous. The gland immediately below the right bronchus is affected more often than that on the left side. The phrenic nerve is occasionally found displaced by the enlarged gland, and through its irritation adds to the coughing. In a number of cases the enlarged gland can be demonstrated by the *x*-ray. French reports the case of a girl, aged seven years, who, though apparently healthy, had had a cough for many months. Examination of the chest was negative, but an *x*-ray of the thorax showed an abnormal, bulging shadow at the root of the right lung, which corresponds to the site of the bronchial glands. It is important to realize this cause in prolonged and inexplicable coughing, as most of these glandular enlargements are tuberculous. This condition would indicate general hygienic treatment and protection from food or cow's milk infected by tuberculous products.

Otitis Media from the Rubber "Pacifier".—W. H. BOWEN (*The Lancet*, 1911, clxxxi, 758), after a long observation of infants in the East London Hospital for Children, believes that many cases of otitis media in infants are caused by the rubber "pacifier" or "comforter." The class of cases he refers to is composed of fairly healthy infants with no attendant infectious disease and with no evidence of adenoids with which to explain the otitis media from which they suffer. As otitis media is usually the result of oral sepsis from mouth breathing due to adenoids, or from an attendant infectious disease, it is fair to argue from analogy that the class of case under discussion is the result of oral sepsis introduced by the "comforter." This article, usually of rubber and attached to the infant by a string or tape, when not in the infants mouth comes in contact with all sorts of unclean things. Being usually moist when dropped, particles of all sorts easily adhere. It is usually reinserted in the infant's mouth without being cleansed. There is also a lamentable practice among some baby tenders to give the "comforter" a preliminary "suck" before putting it into the baby's mouth. It can be plainly seen how easily the child's mouth may become infected in this way. The "comforter" is at fault only in so far as it introduces sepsis leading to catarrhal processes, which spread by the tube to the middle ear, although giving very little, if any, evidence in the mouth, oro-

pharynx, or nasopharynx. Given a "comforter" which is cleaned regularly, never allowed to touch anything dirty, and never placed in the mouth of anyone but the infant, the septic element is eliminated, but this condition of affairs rarely maintains. Where suppuration occurs without this "comforter" to hold as the responsible cause, the cases will be found to be few in number and the cause possibly due to oral sepsis from other causes.

Investigations on Children and Spouses of Paralytics.—F. Plant and M. H. Goering (*Münch med. Woch*, 1911, lviii, 1959) derived the material for their investigations from 54 families, and examined 46 spouses and 100 children of paralytics. In 42 cases the husband was paralytic, in 12 cases the wife. In the 54 families there have been 244 births; 49 of which were miscarriages or stillbirths; 65 died in infancy, and 130 survived; and from these 130 children, 100 were chosen for examination. Of the children, 26 gave a positive Wassermann reaction, and 6 were suspicious, making a probable total of 32 children infected. The majority of these children were under fifteen years, so that it is improbable that they contracted the disease in the usual manner. The Wassermann test was positive in 32.6 per cent. of the spouses, the wives of paralytics showing 31.6 per cent., and the husbands of paralytics showing 37.5 per cent. positive. Of the 100 children, 45 showed physical or psychic stigmata of the disease. Especially frequent were the pale, weak, underdeveloped, children with all sorts of psychopathic impulses, but with no physical signs of central nervous disease. They were almost all timid, shy, whining children, subject to outbursts of rage and an unsound sleep. Twelve such children suffered from severe headaches. The mentality of this class was, however, good. A disposition to lying and stealing was only found in 4 cases. Convulsions during dentition were found in 32 per cent. of the positive cases. Hutchinson's teeth were found in 3 cases and keratitis in 2 cases. Syphilis was diagnosticated clinically in 22 out of the 32 cases with positive Wassermann reactions, and in 23 of the 68 children giving a negative reaction. The question of how long after the apparent cessation of the disease in the parent it can be transmitted to the child is suggestively answered by the histories of 11 families, among whom were 24 children. Five of these showed a positive Wassermann, and of the 5, 1 was born syphilitic four years after the apparent termination of the disease in the parent; 2 were born seven years, 1 nine years, and 1 twelve years after the termination. Syphilis in the father takes precedence over that in the mother, so far as the transmissibility of the disease to the children is concerned. Among the children with negative reactions the time from the father's infection to the birth was from one to twenty-five years. Out of 11 of this class born less than twelve years after the parent's infection, 7 showed physical or psychical stigmata of the disease, while 8 children born after the twelve years limit were found to be sound in these respects. In the 100 cases syphilitic processes in the central nervous system were found in 6 instances, all of which gave the positive Wassermann. Four had paralytic mothers, and 2 had paralytic fathers. It appears that these changes are more common in syphilis originating through the mother than through the father. Unfortunately, in the

majority of all these cases syphilis was not thought of or diagnosticated, and the specific treatment not given. This was also the case among the infected mothers. There is therefore a large field for improvement in the diagnosis and treatment of conditions in children which arise from inherited disease in the parents.

The Therapeutics of Habitual Vomiting in Infants.—Hans Hahn (*Medizinisch. Klin.*, 1911, vii, 1452) offers a method of treating habitual vomiting in infants. This type of vomiting consists in repeated vomiting of food after each feeding, accompanied by no other symptoms referable to the stomach or intestinal tract. This condition, however, is difficult to differentiate from pylorospasm in some cases. In habitual vomiting, however, the peristaltic waves and the rigidity of the stomach wall, together with the pyloric tumor, are absent. Pylorospasm occurs usually during the first six weeks, while habitual vomiting occurs later. The theory is that the two conditions may be associated, or that the vomiting is due to hyperesthesia of the gastric mucous membrane of nervous origin. Clinically this form of vomiting may have to be differentiated from that of meningitis or peritonitis. In the treatment of habitual vomiting a reduction in the quantity of the feeding and the administration of nourishment with a low fat content is usually not successful. Nor is the employment of gastric lavage or the use of narcotics or anesthetics in the form of the bromide, cocaine, eucaine, protargol, or belladonna, followed by any better result. Even the return to breast milk in the typical cases gives no relief, and the child loses weight rapidly and drifts into inanition. It was observed that in such cases some mothers began early to feed their infants on a food of greater consistency than milk, such as ground grits and zwieback in milk, with good results. It was also observed that infants and children without appetite during convalescence from severe illness, or while suffering from chronic conditions, such as tuberculosis, would accept and thrive under a food of greater consistency, while refusing to take liquid diet. Hahn, therefore, tried this form of feeding on cases of habitual vomiting and had very good results, the vomiting often ceasing almost immediately. In some cases the same result was attained in a short time, in others the frequency of the vomiting was greatly reduced. The infants gained in weight and general appearance. The food was prepared by making a porridge of milk and about 5 or 6 per cent. ground grits, so that one liter of the porridge represented about 1000 calories. This amount was divided into 5 or 6 portions for a day's use, so that each feeding represented about 100 calories per kilo of body weight. The same good results were obtained in older children by a change to potato porridge and by adding crumbs of zwieback to the milk. The good results of this form of feeding are probably due to the mechanical action of the more consistent mass on the tendency to contraction of the stomach wall, making it more difficult for the stomach to reject its contents.

The Treatment of Diphtheria.—F. Hoesch (*Deut. med. Woch.*, 1911, xxxvii, 1683) reviews the changes that have taken place during the last few years in the methods of treating diphtheria. Lately, F. Meyer has claimed, and apparently proved, that much larger doses of anti-

toxin can be given with greater benefit than was heretofore believed possible. He has in very severe cases injected at one time as high as 50,000 units, preferably by the intravenous method. In addition, in cases of low blood pressure and collapse, he utilizes Heidenhain's method of injecting adrenalin-normal saline solution intravenously. Both Pospischill and Eckert have reported saving apparently hopeless cases by enormous doses of antitoxin given intravenously. Hoesch has tested these new methods, first laying stress on the primary importance of using the antitoxin at the earliest possible moment, since his tables show a steadily increasing mortality associated with an increasing interval between the incidence of the disease and the administration of the antitoxin. With one exception, Hoesch has never seen a severe grade of diphtheria in a child which had previously been given an immunizing dose of antitoxin, and he believes the practice of giving immunizing doses to exposed individuals to be highly desirable. The intramuscular and intravenous method of giving antitoxin is an improvement over the old subcutaneous method and brings more rapid results. This was shown by Berlin in 34 intravenous injections, in which the temperature was greatly reduced within twenty-four hours, and in 28 similar cases, in which a marked general improvement was observed on the second day. Morgenroth has reported similar good results from the intramuscular method. In Hoesch's series of 325 cases, part treated by the intravenous, part by the intramuscular method, there were 52 deaths, or 16 per cent. Of the 273 intramuscular cases, 33, or 12 per cent., died. Of the 45 intravenous cases, 19, or 42.2 per cent., died. Of the 307 cases treated the previous year by the subcutaneous method, 42, or 13.6 per cent., died. The fact that the intravenous method was used mostly in those cases which were deemed hopeless with the other methods, explains the apparently high mortality with this method. With the intramuscular and intravenous methods the results were noticeable much quicker than with the old method, especially in the effect on single symptoms, such as fever, pulse, and membrane. With the possible exception of nasal diphtheria, Hoesch found no better results from the intravenous than from the intramuscular method, and as the former is often impossible of application in many cases and attended by difficulty in private practice, the latter method of late has been the choice proceeding. That the serum, especially in large doses, acts detrimentally on the heart and kidneys is denied by Baginsky and Heubner, in which decision Hoesch agrees. He also found no advantage in any way in giving larger doses than heretofore in the milder forms of the disease, and therefore gives only 1200 to 2000 units in mild cases. He found practically the same results in the more severe cases, the larger doses, 3000 to 6000 units, having no quicker or stronger effect than the smaller doses. Almost all the cases usually showed increased rate, irregularity, and weakness of the pulse. It was found that the more highly immunized cases usually showed a fairly severe degree of changes in the pulse, many of which remained apparent for long periods of time. The larger doses had also no different effect than the smaller in the laryngeal, severe nasal, and septic forms, and stress is laid on the fact that it is the promptness of its use rather than the size of the dose which counts most. Hoesch finally concludes that the higher doses do not reduce the mortality

below that of the usual doses. If 4000 units are of no avail, then higher doses will leave no better effect. Repeated doses in larger quantities and total doses up to 27,000 units in all the more severe forms have never shown any better results than the more moderate doses. The use of adrenalin intravenously is only justified after all other usual measures of stimulation fail. Normal saline solution, intravenously, is of no benefit in cardiac trouble from diphtheria. Caffeine and camphor have proved the best stimulants in this condition.

OBSTETRICS

UNDER THE CHARGE OF

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The Treatment of Antipartum Hemorrhage.—Herman (*British Med. Jour.*, September 30, 1911) believes that the hemorrhages of pregnancy are made possible by the existence of the placenta. Hence the treatment of this hemorrhage must be conducted with reference to the management of the placenta. So far as accidental hemorrhage is concerned, he believes it of great importance to distinguish between internal and external hemorrhage, which he styles concealed and revealed. In external or revealed hemorrhage, the vessels are torn near the edge of the placenta. The blood separates the chorion from the decidua and escapes through the os uteri. This process differs in duration with different cases, and if the blood escapes slowly it will clot, and the discharge will be a serous, watery fluid. Revealed hemorrhage is far less dangerous than concealed hemorrhage, and is by no means infrequent during pregnancy. In probably less than one case in 100, some form of accidental hemorrhage takes place. In concealed hemorrhage, the utero placental vessels are torn through in the central part of the placenta and blood is effused between the placenta and the uterus. Where the edge of the placenta is not detached, the blood which remains between the uterus and placenta bulges out the uterine wall into a hard, firm tumor. The uterus will readily become distended gradually, but sudden distention produces great pain and often shock, the amount of collapse being out of proportion to the amount of blood poured out. In some cases, this blood remains in its original situation until delivered, but more often when the hemorrhage is at first internal, the effused blood overcomes the adhesion between the placenta and uterine wall, and escapes externally. The pressure on the uterine wall and the effused blood weakens the contractile power of the uterus and favors dangerous postpartum hemorrhage. Herman does not believe that tamponing the vagina tightly is an efficient or correct treatment for such hemorrhage. As the vagina is a dilatable canal, no tampon remains tight very long, and the effort to make it so results in great pain and suffer-

ing to the patient. The one benefit derived from the tampon is the fact that it stimulates the uterus to contract, and thus assists in bringing about the termination of pregnancy. Herman believes that pressure upon a dilated bag is best in these cases, and that the silk bag of Champetier de Ribes is best for this purpose. In every variety of bleeding from the placental site the natural way to check this bleeding is by uterine contraction. While the uterus cannot perfectly contract until it is empty, the tension within the uterine wall is immediately lessened by rupturing the membranes. A tight abdominal binder may also be of some assistance. If the pelvis is ample, and the child small, remedies addressed to stimulating uterine contraction may be given. In cases where hemorrhage is severe, and the os uteri so little dilated that the patient's life will be probably lost before delivery can be effected, abdominal hysterectomy is advised. Herman suggests opening the abdomen, tightening the ovarian and uterine arteries on both sides, then emptying the uterus and performing hysterectomy, leaving the ovaries if they are normal. If the patient is a primipara, he suggests Cesarean section, leaving the uterus, but tightening the uterine arteries before opening the uterus. He is strongly opposed to rapid opening of the cervix in placenta prævia by any form of dilator or by vaginal Cesarean section. In placenta prævia he would bring down the leg and breech of the child by the Braxton-Hicks method and wait for the spontaneous expulsion of the fetus. In placenta prævia cases admitted to hospital he would use the waterproof-silk bag, and, if necessary, he would tie the uterine arteries through the vagina. The writer states that he is told, although he has no personal knowledge of the matter, that in America the uterine arteries have been repeatedly ligatured from the vagina in cases of placenta prævia without any harm resulting, and the same statement is repeated later in his article. This procedure, he says, has been successful in America, and he thinks should be adopted. We supposed that the time had come when radical and extraordinary surgical procedures were not necessarily referred to America and Americans. We are not aware of such a practice among American obstetricians, and in the recent discussion upon placenta prævia, at the last meeting of the American Gynecological Society, May, 1911, this procedure was not even mentioned. We fail to appreciate the benefit or the necessity of the procedure advised by Herman, namely, ligating the uterine arteries before opening the uterus in performing Cesarean section for placenta prævia. In our experience there is far less hemorrhage in Cesarean section for placenta prævia than in other methods of delivery. The uterus can be immediately tamponed to advantage when emptied, and postpartum hemorrhage has not occurred in three cases upon which we have operated. Herman also objects to the vaginal tampon because of the danger of infection by its hurried application in private houses. His warning is timely and is abundantly borne out by other writers. We believe that the majority of opinions today upon this subject are as follows: In a pregnant patient who is not at term, should hemorrhage occur from separation of the placenta, whether it be a private patient or not, treatment consists in dilating the cervix sufficiently, if necessary, to rupture the membranes, followed either by the insertion of the bag or the bringing

down of the leg and breech of the child. In every case no effort should be made to pull the bag or the child through a partly dilated cervix. The patient should be stimulated and the bag or the child should be expelled if possible by uterine contractions. This treatment can usually be carried out, although at considerable risk, in a private house. All cases, however, of severe hemorrhage complicating pregnancy should be transferred to hospital, if possible, because of the danger of infection and the probable necessity for some sort of interference. Where the child is at term and in good condition, or where the cervix is so tightly closed and firm that efforts to dilate it would be followed by serious laceration, the uterus should be emptied by section. In primiparous patients in good condition the uterus should be closed and retained. In multiparous patients not in good condition, hysterectomy should be performed.

Cervical Implantation of the Placenta, with Rupture of the Uterus; Hysterectomy; Recovery.—Goodman (*Jour. Amer. Med. Assoc.*, October 14, 1911) reports the case of a multipara, aged twenty-eight years, who during pregnancy had repeated attacks of pain in the right lower portion of the abdomen. After one of these attacks, which was especially severe, the patient had syncope, distention of the abdomen, and a failing pulse, with great pain. On examination, the patient was blanched, the abdomen distended with fluid, and the pulse imperceptible. Very faint fetal heart sounds could be heard. On vaginal examination, there was tenderness and bogginess in the vaginal tissues about the cervix. A provisional diagnosis of ruptured ectopic gestation was made, and the patient taken to the hospital, and section performed. On opening the peritoneum, fluid and clotted blood was found and a large fluctuating tumor, which seemed to be wedged into the pelvis. This proved to be a pregnant uterus, with a thinned anterior wall which had ruptured near the left broad ligament. The appendages were normal in appearance. Hysterectomy was performed, and it was found that the placenta was attached very low down at the upper extremity of the cervix. The uterus was delivered with the placenta attached and the abdomen closed without drainage. The patient made a prompt recovery. On further examination, the pelvis was not contracted, and on examining the specimen, it was found that the lowermost portion of the uterus showed chorionic villi lining the uterine canal. The placenta began just below the insertion of the uterine vessels, and the placental site was below the isthmus; its development took place within the cervical canal. As pregnancy had reached a period of five months, there was not room for the uterus to expand, and the uterus had ruptured where its wall had been thinned by the chorionic villi.

Salvarsan in Pregnancy and the Puerperal Period.—Langes (*Wien. med. Klinik*, No. 20, 1911) reports the results of treatment by salvarsan in 8 pregnant women and 12 puerperal patients, in whom the Wassermann reaction was positive. The remedy was given by intravenous injection in doses of 0.3 gram, and by subcutaneous or intragluteal injection in doses of 0.3 gram to 0.6 gram. The intravenous injections gave rise to no unpleasant effects, except slight fever lasting

a few hours. The other two methods caused infiltration and pain. The Wassermann reaction showed that the intravenous method is more prompt and efficient. The 8 pregnant patients were all in the latter part of gestation, and in them the specific process was latent. In 5 cases one injection sufficed, and in 3 a second was given. The injections did not bring on labor, and the child showed no evidence of syphilis, the characteristic reaction being absent. There was one case of syphilis of the nervous system which had been treated outside of the hospital and in whom labor came on twenty-four hours after the treatment. The fetus was seven months advanced, macerated, and syphilitic. Among the puerperal cases, 8 had latent syphilis, one secondary; one patient had been delivered of a seven months' macerated fetus; one had aborted at five months; the others had gone to term, but one child having a positive reaction at birth, and one dying from syphilitic pemphigus. The indirect treatment by salvarsan was effective in the case of the child giving a positive reaction, for the reaction changed at the end of three weeks. It is evident that the remedy cannot be given too early in pregnancy when symptoms of syphilitic disease are present. To prevent abortion and secure the birth of a healthy non-specific child, the treatment should be followed by mercury and the reaction used to note the result of the treatment. These observations would reverse Colles' law, that mothers of specific children are immune if symptoms are absent. The serum test shows that such mothers are to be considered as infected.

Shall Portions of Placenta Retained after Full-term Labor Be Removed or Allowed to Remain?—Hörmann (*Monatssch. f. Geburts. u. Gynäk.*, 1911, Band xxxiv, Heft 4), considers this question at some length and discusses Winter's paper, in which the view is expressed that the retention of pieces of placenta aside from the membranes, or pieces of the ovum, may occasion severe infection. In his experience he has seen no case in which the emptying of the uterus by artificial means, and the removal of retained placenta, has converted a mild into a severe fever, or caused the death of the patient. On the contrary, 2 fatal cases under his observation perished through excessive loss of blood because delay was practised in removing the retained placental portion. He believes that it is not so much the danger of infection as the perils following hemorrhage which indicate the prompt and complete removal of retained portions. Every puerperal patient who has retained placenta is in danger of severe bleeding, and should be considered as in a critical condition. In 36 cases, such material was removed by the fingers in 23; by the dull curette in 6; by placental forceps in 3; by the uterine tampon in 1; and by irrigation of the uterus in 3. The greater portion of cases having retained parts of placenta recover without fever—in the Königsburg clinic, 59 per cent. Severe infection may accompany such cases, which must be referred to the retained placenta. The proposition to await the spontaneous expulsion of this material is not practical, for in 80 per cent. hemorrhage obliges the physician to interfere. An additional means of diagnosis would be a bacteriological examination in each case to determine the presence of infection and the nature of the infective germ before deciding upon operation.

GYNECOLOGY

UNDER THE CHARGE OF

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Suicidal Tendencies of Gynecological Origin.—Bossi (*Zentralbl. f. Gynäk.*, 1911, xxv, 1265) believes that not less than 50 per cent. of the cases of suicide among women are of gynecological origin. By this he does not mean that the gynecological lesions are necessarily the fundamental cause, but that they release the trigger, so to speak, and actuate a tendency which by their mere presence they have accentuated. He has not found it to be the severe, or even the painful conditions that produce most of these cases. Suicidal tendency is not especially marked among sufferers from carcinoma, even though aware of the hopelessness of their condition, nor in cases of large cysts or fibroids, or of painful adnexal disease. It is, on the other hand, seen most markedly in patients suffering from chronic infectious metritis, especially when this is combined with uterine displacements. Bossi believes that retroversion and angulation of the uterus, with consequent infectious endometritis, is responsible for most of the cases of suicidal tendency of gynecological origin, and he considers this attributable entirely to the toxemia caused by the infection. This explains also the well-known fact that a suicidal tendency, where it exists at all, is always especially strong at, or just before, the menstrual periods. In addition to the general psychic unbalance present at these times there is an increased congestion of the genital organs, and a consequent increased production of toxic substances owing to the increased blood supply of the organs in question. Increased quantities of these toxins are therefore thrown off into the circulation at these times, and are carried to the nervous centres. The effect of this is frequently sufficient to cause a temporary complete loss of mental balance, and to drive the subject to the accomplishment of an act which would be repulsive to her at any other time. The proper treatment of the gynecological condition in these cases Bossi considers to be a certain prophylaxis against this occurrence, and he quotes in illustration a number of most striking cases of women who had made repeated attempts at suicide, some of whom had been confined for long periods of time in institutions on this account, who were completely cured by operation, and were able to again become useful members of their families.

Painful Nephritis and its Surgical Treatment.—Rochet (*Lyon Chirurgical*, 1911, vi, 249) divides cases of nephritis associated with pain into two general classes: (1) Those in which suppuration of the urinary passages is present, and the urine contains pus. (2) Those in which there is no infection, or at most an insignificant one; the urine is clear, or if at times a cloudiness is present this is due to urates,

phosphates, etc., and not to pus. Many of the cases in class (1) are probably merely ones of pyelitis or pyelonephritis, in which pain is the rule, and these are to be sharply differentiated from class (2). These cases of slight suppuration are interesting, however, as generally the pain is not proportional to the amount of suppuration. It is probably due in these cases to the action of an intermittent congestion of a chronically inflamed kidney beneath a capsule which constricts it, or to the existence of a fibrous perinephritis which prevents free motion of the kidney in respiratory or abdominal movements. Generally, one or both of these conditions is found at operation. In the second category there is no marked infection, and the pain must, therefore, be considered more purely nephritic in origin. It may be dull and constant, or sharp and shooting in character, and in all cases reported by Rochet was limited to one side. He reports 10 cases of this condition in all, 3 of these falling in class (1), the others in class (2). In 2 of the latter, both occurring in young girls, an interesting condition was found, in that in each case urine from the affected side produced tuberculosis in guinea-pigs, and yet at operation, the kidney appeared perfectly normal. In both cases nephrotomy was performed, but no tuberculous lesions found. The surfaces of the kidney were in each case brought together by sutures; both patients made a good recovery, both have been entirely relieved of their pains, and neither has developed any signs of tuberculosis. One case has gone through a normal pregnancy, and has been under observation for three years since operation. The 3 cases falling in class (1) showed the presence of dense adhesions and thick, fibrous masses around the kidney. In the other 5 cases no definite cause for the pain could be found; in 1 no demonstrable renal or perirenal lesions were present; in 1, there was a slight sclerosis of the perirenal tissue; in 1 there was merely an interstitial nephritis, and in 2 the kidney was large, congested, the color of wine dregs, and showed subcapsular strangulation. The operations employed in the treatment of these 10 cases were as follows: "Decortication" (removal of fatty capsule), 2; decapsulation, 2; nephrotomy, 5; nephrectomy, 1. All cases were cured symptomatically, all but 1 having been followed from one to five years since operation. In nearly all cases albumin was present in the urine of the affected side before operation; since operation, this has in most of the cases persisted, but in decreased amount. It is suggestive that, of the 7 cases of the second class, 6 occurred in women of dicidedly neurotic tendency.

Use of Silver Wire in Nephrotomy.—The results of a series of experiments on dogs, in which nephrotomy was performed by the use of silver wire instead of the knife, are reported by Derge and E. K. Cullen (*Surg., Gyn., and Obstet.*, 1911, xiii, 365). Their technique, the various steps of which are illustrated by Brodel's incomparable drawings, is to pass a No. 3 or No. 4 silver wire, by means of a suitable needle, into the pelvic portion of the kidney, and then by a see-saw motion to gradually draw it out through the kidney substance to the surface, firm countertraction on the kidney being made by an assistant. In this way, the entire kidney, or as much of it as is desired, may be laid open, according to where the needle is introduced and

brought out. Derge and Cullen claim that much less hemorrhage is caused by this method than by the use of the knife, since many of the branching vessels are rather pushed aside by the wire than cut through, the cut being made in the direction in which they slope by a smooth, yielding surface, whereas the sharp, hard edge of the knife, passing in the reverse direction, simply cuts through all vessels in its path. This claim is supported by two series of experiments, in one of which transverse, in the other longitudinal cuts were made in the kidneys. It was found by accurate measurement of the hemorrhage for a period of twenty seconds that in both series the ratio of the amount of hemorrhage in the wire-cut to that in the knife-cut cases was about 1 to 2. In the former the hemorrhage was almost entirely venous, with very rarely a small spurting vessel, and was easily controlled by mere approximation of the surfaces, or by hot gauze; in the latter, spurting vessels were often seen on the cut surface, and at times compression of the artery had to be resorted to to control the bleeding. One month after operation the dogs were killed, and the kidneys examined microscopically. It was found in all cases that the infarct, and consequent destruction of kidney substance, occurring after the knife operation was much larger than after the use of the wire. In conclusion, a series of cases are reported in which this method has been used on human subjects by Halsted, Kelly, and T. S. Cullen, with, on the whole, very favorable results so far as hemorrhage is concerned.

End Results of Nephrectomy in Renal Tuberculosis.—Israel (*Folia Urologica*, 1911, vi, 257) presents his conclusions based upon the study of 1023 cases of nephrectomy for renal tuberculosis, 170 of these being cases of his own; the information concerning the others was obtained through personal communication with some twenty of the best-known European urologic surgeons. His most important conclusions drawn from this large material may be summarized as follows: There is no spontaneous cure of renal tuberculosis; tuberculin treatment does not cure it; the only thing that does cure it is early nephrectomy. The total mortality, *i. e.*, both "early" (within six months of operation) and "late," amounts to 25 per cent. of all cases operated on, so that three-fourths of the patients are saved by the operation. Nephrectomy in cases of unilateral tuberculosis prevents its development in the opposite kidney in most cases, but a healthy kidney will become infected from a tuberculous one which is not removed much more frequently than from any other focus. In bilateral kidney tuberculosis nephrectomy should be done only where there is severe destruction of one organ with only an incipient affection in the other, associated with frequent, severe hemorrhages, or intolerable pain. In cases of unilateral tuberculosis associated with Bright's disease, nephrectomy should be done only if the danger from the tuberculous kidney seems to be greater than that from the lack of secreting parenchyma. Toxic conditions of the opposite kidney, other than Bright's, generally clear up after a nephrectomy. In unilateral tuberculosis the bacilli disappear from the urine in three-fourths of all cases, this being determined by inoculation. They may persist, however, without producing symptoms for as long as seventeen

years, these patients being comparable to typhoid carriers. The bacilli disappear more frequently than does the inflammation of the bladder mucosa, which is completely cured in but 43.5 per cent. of the cases. Tuberculosis of the ureter will be cured spontaneously after nephrectomy in the majority of cases; ureteral fistula develops in 11.5 per cent., but nearly always closes within four years. The method of treating the ureter does not seem to have any marked influence on the frequency of fistula formation. A subsequent pregnancy has no more effect on the remaining healthy kidney than on the kidneys of normal individuals, but neither men nor women should be allowed to marry after operation until a permanent disappearance of tubercle bacilli from the urine has been demonstrated.

Instrumental Dilatation of the Ureter.—Since the opening of the ureter into the bladder is the narrowest part of its course, it is here that the chief obstacle is presented to free drainage in cases of infection of the upper portions of the urinary tract. By means of his aëro-cystoscope, KELLY (*Can. Med. Assoc. Jour.*, 1911, i, 849) has been able to pass graduated bougies in the course of one or several sittings into the ureteral orifice, and to thereby dilate this up to 6.75 mm. in diameter. For the larger sizes he uses chiefly olive-tipped bougies graduated in thirds of a millimeter. In addition to being of use in the treatment of pyoureter and pyelitis, this procedure can be utilized to obtain the passage of a stone *per vias naturales*, Kelly employing for this purpose an alligator forceps which he passes for 5 cm. or more up the dilated ureter to grasp a stone which is out of sight, but which has been previously located by *x*-rays, sound, or wax-tipped bougie.

DERMATOLOGY

UNDER THE CHARGE OF

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Extramammary Paget's Disease.—M. B. HARTZELL (*Journal of Cutaneous Diseases*, August, 1910) gives an interesting paper on this rare disease, illustrated by cases and personal observations on histopathology. Of the 18 cases referred to, no less than 9 occurred on the external genitalia, and 5 affected the glans penis. It will thus be noted that this disease is by no means to be regarded as confined exclusively or largely to the female breast and nipple and areola in particular, as first described by Paget, and subsequently designated by other writers as "Paget's Disease of the Nipple." The pathological anatomy is entered into with original observations, illustrated by microphotographs.

Imagined Parasites, Atoxyl, Blindness.—Juan de Azua (*Revista Clinica de Madrid*, November 1, 1910) reports the case of a physician who was addicted to morphine and cocaine, the latter suggesting to him the idea of parasites upon the skin. First, mercurial inunctions were employed for the imagined parasites, followed by stomatitis, then for thirty-three days injections of atoxyl, which was followed by total blindness (papillary atrophy).

Rhinoscleroma Cured by X-ray Treatment.—S. Pollitzer (*Journal of Cutaneous Diseases*, August, 1910) records an instance of this distinctly rare disease (very seldom encountered in the United States), occurring in an Austrian woman, which was cured by the *x*-rays, three years having elapsed after cure without recurrence. Distinct improvement was recorded two weeks after beginning the treatment. (Cases of cure by other observers, especially in Austria, have been recorded from time to time during the last decade.—L. A. D.)

The Treatment of Erythematous Lupus with the X-rays.—Moberg (*Archiv f. Dermatologie u. Syphilis*, Band cvii, Heft 1 to 3) has treated 18 cases of erythematous lupus of varying degrees of severity with the *x*-rays, and is thoroughly convinced that this agent has an undoubted effect upon the disease. It does not exert a specific effect upon the malady such as it exhibits in epithelial new formations, such as verruca and epithelioma; and in order to obtain effects superficial or deep destruction of the treated parts must be produced. In 6 out of the 18 cases treated a cure without recurrence was obtained; a cure, but followed by recurrence, in 4 cases; in 6 cases, while the cure was not complete, a very inconsiderable portion of the disease was left; in the last 2 cases the favorable effect of the treatment was quite clear, but the patients ceased attendance too early. The author is quite convinced that, although by no means an ideal treatment, the *x*-rays have a very important place, along with other local treatment, in the therapeutics of this most obstinate disease.

Eczematoid Ringworm.—Whitfield (*British Journal of Dermatology*, February, 1911), under the title, "Some Notes on Tinea Circinata," calls attention to a form of ringworm occurring on the hands and feet which is usually indistinguishable from an acute vesicular eczema without the aid of the microscope, and which is, in consequence, very liable to be mistaken for this latter affection. Whitfield, a few years ago, called attention to this form of ringworm, and has since been collecting new cases; he now reports 7 additional ones. In these 7 cases there was a vesicular eruption upon the hands or feet, and the presence of the trichophyton fungus was demonstrated in all of them. In the treatment of this form of ringworm Whitfield has found an ointment containing 3 per cent. of salicylic acid and 5 per cent. of benzoic acid very effective.

New Researches upon the Etiology of Alopecia Areata.—Sabouraud (*Annales de Dermatologie et de Syphiligraphie*, 1911, No. 2), from a recent clinical study of 100 cases of alopecia areata taken at random, concludes as follows: In 22 per cent. of the cases of alopecia areata, at least,

there exist several cases in the family, either in the direct line or in the collateral branches. In 11 per cent. the affection is directly hereditary, being more frequent in the paternal than in the maternal line. In an equal number of cases the disease is present in two collateral branches. Cases are less frequent in collateral branches of the preceding generation, but do occur. Whole families are occasionally observed which are affected by the malady, even for three generations. Sabouraud especially emphasizes the fact that in 100 cases taken at random the affection is hereditary in at least 22.

Eosinophilia in Scabies.—Kolmar (*Journal Cutaneous Diseases*, June, 1911), studying 18 cases of scabies observed during its occurrence in an institution for children, found that there was a fairly well-marked eosinophilia, the eosinophilous cells being increased in number relatively as well as absolutely. The degree of eosinophilia appears to depend upon the severity of the disease, being most marked during the acme of the eruption, gradually reaching the normal with the cure of the malady. Kolmar also noted a mild leukocytosis, varying in amount according to the severity of the affection.

Gonorrheal Hyperkeratoses.—Arning and Meyer-Delius (*Archiv f. Dermatologie und Syphilis*, Band cviii, Heft 1 and 2) report a number of cases of gonorrhea accompanied by cutaneous symptoms, the most interesting of which was a hyperkeratosis, usually upon the hands and feet. In conclusion, Arning and Meyer-Delius find that there is a definite form of gonorrheal general infection characterized by multiple subacute, non-ankylosing arthritis, endogenous conjunctivitis, and a third symptom, the so-called gonorrheic keratosis. The last appears most frequently under the form of a balanitis circinata, less often upon the hands and feet, and upon other portions of the cutaneous surface. The keratosis has a preliminary vesicular stage which is followed later by parakeratotic crust formation. Transitions to other forms of gonorrheic exanthemata are observed. Rost (*Dermatologische Zeitschrift*, Band xviii, Heft 3) likewise reports 3 cases of gonorrheal keratosis associated with universal ankylosing arthritis. In concluding his report he remarks that such hyperkeratoses are infrequent in gonorrhea, and that they are almost always associated with polyarticular, subacute, tolerably severe inflammation of the joints, which may go on to ankylosis. Besides the skin and joint symptoms, there may be severe general symptoms, cachexia, neuralgias, and muscle atrophy. The appearance of the exanthem, like the arthritis, is not associated with manifest gonorrhea, but may arise from latent foci even after several years.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Beriberi and Unpolished Rice in the Philippines.—HEISER (*Jour. Amer. Med. Assoc.*, 1911, li, 1237 to 1238) reports excellent results from the use of unpolished rice in the Philippine Islands. Prior to February, 1910, polished rice was commonly used in the Culion leper colony. The deaths from all causes between February, 1909, and February, 1910, were 898 of which, 309 were due to beriberi. From February, 1910, to February, 1911, unpolished rice was used, and there were 369 deaths, a reduction of over one-half the death rate for the previous year. It is significant that there were no deaths from beriberi during this interval following the use of unpolished rice. At the end of January, 1910, about 50 patients remained in the hospital of the colony undergoing treatment for beriberi. Each of these patients received daily, in addition to the regular food allowance, 15 grams of rice polishings, and improvement was noticed in all except 2 very advanced cases, which subsequently died. Within two weeks following this treatment, however, the cases were so far recovered as to be able to leave the hospital, and within a month all were pronounced cured. These results have been so striking that the government has drafted a bill providing for the general use of unpolished rice; that is, rice containing at least 4 per cent. of phosphorus as phosphorus pentoxide, and the levying of a tax upon polished rice which makes its sale practically prohibitive. With such an array of facts it would seem that a definite advance has been made in the study of beriberi.

BREAUDAT and DANIER (*Annales de l'Inst. Pasteur*, February, 1911, No. 2) report from the Pasteur Institute at Saigon in Indo-China that rice bran seems to remove the cause of beriberi and prevent its development. They gave the bran in the form of pills mixed with syrup and peppermint, about 40 grams of the bran being thus added daily to the ordinary food. As a prophylactic it was found that no case of beriberi developed among 49 native soldiers who took the bran, while 17.4 per cent. of 311 controls developed the disease.

The Danger in Drinking Milk from Cows with Udder Tuberculosis.—WEBER (*Tuberkulose Arbeiten aus dem Kaiserlichen Gesundheitsamte*, 1910, Heft x) reports the results obtained from an investigation extending over four years (January, 1905, to April, 1909) by the Imperial Board of Health of Germany; 113 separate investigations were made including 628 persons (284 of whom were children, 335 were adults,

and 9 of unstated ages), all of whom had undoubted opportunities of consuming milk or milk products from cows having tuberculosis of the udder. The evidence presented is not equally vaulable in each investigation; in 44 of the 113 investigations cited the milk was either heated, used in coffee or tea, or mixed with milk from apparently tuberculous-free cows before it was consumed. Weber has analyzed the data presented and has divided the persons studied into four groups. Group 1: Instances in which infection with the bovine tubercle bacillus (Perlsuchtbazillen) has followed the drinking of raw milk of a cow having a tuberculous udder. Group 2: Instances in which there is reason to believe that a bovine infection exists or has existed, but in which no definite conclusions can be drawn because of the lack of a careful bacteriological study of the case. Group 3: Instances in which bacteriological examination has failed to demonstrate tubercle bacilli, or in which the organisms were demonstrated to be of the human type. Group 4: Instances in which individuals have remained apparently well in spite of drinking raw milk or raw milk products from cows with tuberculous udders. Group 1: Instances of apparent infection with bovine tubercle bacillus; 2 cases. Case 1: Cow had udder tuberculosis as well as a generalized infection. Father, mother, and three children, aged five, four, and one year and ten months, respectively, drank the milk of this cow, both cooked and uncooked, mixed with that of another, apparently healthy cow. Family healthy; youngest child had a movable swelling in the left submaxillary region which, upon examination, was found to contain caseous purulent pus. Microscopic examination showed the presence of bovine tubercle bacilli. Animal experiments confirmed results. Case 2: Cow with tuberculous udder. Milk mixed with that of another cow drunk unheated for at least three months after the cow was known to be tuberculous. Family consisted of father, mother, seven children, aged twelve, nine, eight, seven, four, three, and one year and three months, respectively. All healthy except youngest, who had purulent lymph glands on left side of the neck. Bovine tubercle bacilli isolated from the lymph glands and proved to be of bovine type by inoculation into experimental animals. Group 2: Suspicion of bovine tubercle bacilli infection with incomplete bacteriological evidence. Seven cases in all. Judgment reserved. Group 3: Suspected cases in which infection with bovine tubercle bacilli could be ruled out either by exclusion of tuberculosis or by the finding of human tubercle bacilli. This group of cases, which cannot be suitably summarized in a few words, contains the most difficult ones to diagnosticate—indeed, it would appear that the evidence brought forward for some of them is hardly conclusive enough to separate them from the second group, in which the bacteriological evidence is insufficient, but in which the clinical symptoms suggest strongly tubercle infection. Group 4: Cases in which the consumption of milk and milk products was not followed by tuberculosis. The relatively large number of cases reported in this group are at once interesting and instructive. The case histories show a careful study of many families using milk from cows with tuberculous udders, even for considerable periods of time, yet remaining well as far as can be determined clinically. The very considerable number of children using such milk is particularly worthy of notice, because milk known to contain bovine tubercle bacilli

formed a very considerable item in their diet. Weber gives the following summary: 360 persons, of whom 151 were children, 200 adults, and 9 of unknown age, used milk or milk products, butter, buttermilk, sour milk, and cheese, which came from cows having undoubted tuberculosis of the udder. Of all these 360 people, only two were shown by actual animal experimentation to have infections with the bovine tubercle bacillus. These two positive cases were children having tuberculous neck glands. It was possible to show, furthermore, that both these children had drunk milk from cows suffering with bovine tuberculosis, and that these cows certainly had tuberculous udders. The milk of these cows was drunk in the first case a year and a half and in the second case several months after the cows were known to be sick. In each instance the udder tuberculosis was extensive, in one cow all four quarters of the udder were infected. The milk of these tuberculous cows was mixed with that of a second apparently healthy cow in each instance before it was consumed. In both cases it was found that the other members of the family were perfectly healthy, although they had drunk the same milk uncooked. In both families the tuberculous child was the youngest. Six other children and 1 adult had glandular swellings in the neck, and in 4 other children and 1 adult who had drunk milk containing bovine tubercle bacilli there was a strong suspicion on the part of the attending physician that abdominal tuberculosis was present. It is to be noticed, however, that in the 4 latter children the clinical symptoms were recessive, while Weber considers that in the adult it is very improbable that the disease could be attributed to the drinking of milk. In 1 child, further, there was a well-defined history of scrofula. In another series of 360 people, in whom it was shown that they drank the milk of cows with tuberculous udders or consumed uncooked milk products made from the milk of these cows, there were 12 children and 1 adult with swellings of the lymph glands of the neck. In these 12 children and the adult no bacteriological examination was made, and consequently it is impossible to state definitely whether these glandular swellings were of tuberculous origin. The writer concludes, finally, that the danger which men undergo through the consumption of uncooked milk and milk products of cows having tuberculosis of the udder is similar to the danger which men having well marked pulmonary tuberculosis exhibit for their fellowmen, although very much less. It seems fair to assume from the statistics presented above that the danger from drinking uncooked milk and milk products of cows with tuberculous udders is surprisingly small.

The Vaccination of Cattle Against Tuberculosis.—Theobald Smith (*Journal of Medical Research*, September, 1911, xxv, Part ii) studied the pathogenic effect of certain cultures of the human type of tubercle bacilli on calves. This work is the continuation of an investigation conducted under the auspices of the Massachusetts Society for Promoting Agriculture. The first paper appeared in the *Journal of Medical Research*, June, 1908, vol. xviii, in which it was shown that vaccination of calves with cultures of the human type of tubercle bacillus leads to a relatively high resistance to the bovine type of tubercle bacilli. The work presented here represents a carefully planned

and executed study of the effects of vaccinating young calves with cultures of human tubercle bacilli in order to test the practical value of Behring's bovo-vaccination. The pathogenic effects of certain human tubercle cultures for calves are specifically considered. Non-tuberculin reacting calves only were used for the experiments, and bull calves were excluded. Suitable precautions were instituted and maintained to prevent infection with bovine tubercle bacilli. The vaccines used were of such strength that a cubic centimeter of normal saline solution contained 1 cg. of moist tubercle bacilli. Injections were made into the right jugular vein. In all, 14 calves were vaccinated. Of these, 6 died or were killed and showed lesions post mortem; 8 survived the first inoculation, remaining in good health, and of these 8, 5 received a second injection and survived in good condition, and of the latter 5, 1 received a third injection which was well borne. Of the 6 calves that died, all received the same vaccine, Human No. XXIV, which appeared to be unusually virulent for calves; 4 calves, however, successfully endured this same strain (Human No. XXIV), and 2 of these animals received a second injection, one of the latter being inoculated a third time without harmful results. Dr. Smith concludes as follows: (1) Calves may succumb to a tuberculous pneumonia not seen in the spontaneous bovine disease after an intravenous injection of certain cultures of the strictly human type. The initial rise of temperature usually appears within ten to fifteen days, and death may ensue after one to two months. Tuberculosis of both eyes, with complete blindness, may result. (2) The culture used in the foregoing experiments which proved fatal for calves (Human No. XXIV) was rather below than above the average virulence of the human type for rabbits. (3) The sensitiveness to tuberculin may persist in calves from eight to twelve months after an injection of living bacilli of the human type. (4) A second and third larger dose of the same strain is quickly and easily disposed of by calves which have survived the first dose.

The Isolation of B. Typhosus from Butter.—D. H. Bergey (*Journal of Medical Research*, September, 1911, xxv, 231) recovered the typhoid bacillus from samples of butter suspected of causing an epidemic of typhoid fever in an institution. The technique employed was sufficient to warrant the diagnosis of B. typhosus.

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